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THE DEVELOPMENT OF THOUGHT ON THE ETIOLOGY OF PERNICIOUS ANEMIA*†

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In the light of recent advances in our knowledge of pernicious anemia, it is evident that as early as 1833 important observations bearing on the etiology of this disease were recorded by William Beaumont. Among other things he said:

"In febrile diathesis, or predisposition, from whatever cause—obstructed perspiration, undue excitement by stimulating liquors, overloading the stomach with food, fear, anger, or whatever depresses or disturbs the nervous system—the villous coat becomes sometimes red and dry, at other times pale and moist, and loses its smooth and healthy appearance; the secretions become vitiated, greatly diminished, or entirely suppressed; the mucous coat scarcely perceptible; the follicles flat and flaccid, with secretion insufficient to protect the vascular and nervous papillae from irritation. . . . When considerable, and particularly, when there are corresponding symptoms of disease, no gastric juice can be extracted, not even on the application of alimentary stimulus. . . . Whenever this morbid condition of the stomach occurs, with the usual accompanying symptoms of disease, there is generally a corresponding appearance of the tongue."

In 1849, in an introduction to "The Constitutional and Local Effects of Disease of the Suprarenal Capsules," Thomas Addison gave the first description of what we now recognize as the clinical picture of pernicious anemia. Twenty-six years later, Biermer, apparently unaware of Addison's earlier account, described the same condition. In Continental Europe, the disease is still known by his name.

The association of atrophy of the stomach with pernicious anemia was first noticed by Samuel Fenwick in 1877. He stated at that time that he lacked the means to collect and subject to chemical tests the gastric fluid during life. Nine years elapsed before the absence of free hydrochloric acid in the gastric secretion was demonstrated by Cahn and Von Mehring. In the same year, 1886, Henry and Osler described the pathology of authenticated cases. Levine and Ladd, in 1921, in a study of 143 cases found that free hydrochloric acid was lacking in all of them and concluded that this was an invariable part of the disease picture. Since then, however, well-established cases with detectable free hydrochloric acid have been reported by Castle, Heath and Strauss; Barnet; and Harvey and Murphy. Shaw and Hurst, and McPeak and Neighbors have reported authentic instances in which free hydrochloric acid returned following treatment.

Early theories of the etiology of pernicious anemia held that the disease was due to degeneration of gastric tubules caused by abuse of alcohol and food and that this resulted in inadequate digestion. This idea was supported by the development of pernicious anemia following total gastrectomy. However, not all cases of total gastrectomy have developed pernicious anemia, and experimentally gastrectomy in dogs and other animals is not followed by a picture resembling the disease. In 1899, Neusser offered the alternate hypothesis, that the gastro-intestinal changes were secondary to a systemic disturbance.

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* Read before the Section on Internal Medicine of the Society, October 23, 1936.

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By means of metabolic studies, Strauss, in 1900, could discover no unusual alteration in the utilization of protein and fat, but in 1934, Griffiths and Maltby independently demonstrated that there was deficient digestion of beef protein by the gastric juice of patients with pernicious anemia.

Prior to the epochal announcement of Minot and Murphy in 1926, the disease was generally believed to be a hemolytic anemia, and Arthur Hurst's explanation of the etiology was most generally accredited. He believed that as the result of achlorhydria two things happened: The antiseptic action of the gastric juice was lost, and proteins were incompletely digested in the stomach. This permitted abnormal bacterial activity on these proteins in the intestinal tract which resulted in the liberation of hemolytic and neurotoxic factors leading to the prominent manifestations of the disease. However, in 1928, Davidson's critical studies of gastro-intestinal bacteriology before and after specific treatment failed to support Hurst's idea.

The modern era of pernicious anemia may be said to have had its beginning in 1925. In studying the influence of various substances on the regeneration of hemoglobin in dogs made anemic by repeated bloodletting, Whipple obtained maximal results when liver and kidney were added to the basal diet. Although the anemia of Whipple's dogs was hypochromic in type and bore no resemblance to pernicious anemia, Minot and Murphy decided that a diet including liver would be worth trying in pernicious anemia. The remarkable results that followed revolutionized not only our treatment but our concept of the disease. It started a remarkable wave of research which in the succeeding 10 years has added more to our understanding of the disease than had been learned in the previous 100 years.

In 1927, Cohn, Minot and their coworkers, succeeded in preparing a protein-free liver extract containing but 2 per cent of the original material. McCann, in the following year, demonstrated the efficacy of kidneys. In the next year, Sturgis, Isaacs and Sharp reported that whole chopped hog stomach contained an antianemic factor comparable to that in hepatic tissue.

On the theory that a deficiency in gastric function was responsible for the disease, Castle and his colleagues devised a series of ingenious experiments in an attempt to determine the exact nature of this deficiency. A number of medical students were induced to eat 200 grams of beefsteak and at the end of an hour regurgitate the contents of their stomachs. This material, neutralized and partially disguised, (Honi soit qui mal y pense) was then introduced into the stomachs of patients with pernicious anemia. This induced a remission of the disease which was in every respect similar to that brought about by the liver diet. He was able to duplicate these results when normal gastric juice and beefsteak were permitted to interact in vitro. However, when the beef was permitted to interact with either hydrochloric acid, hydrochloric acid and commercial pepsin, or heated gastric juice, the results were negative. From these experiments, Castle was able to conclude that the substance in gastric juice which interacted with the beefsteak was something other than its commonly recognized constituents. He proved that an interaction actually took place by feeding to the patients with pernicious anemia the beefsteak in the afternoon and the medical students' gastric juice the following morning. The results were negative. The experiments had, up to this point, suggested that normal gastric juice contained something which acted upon beef, but it was possible that either saliva or regurgitated duodenal material contributed something to the phenomena. It was easy to eliminate saliva from consideration by the simple experiment of incubating saliva in place of gastric juice with beef. However, more difficulty was encountered in experiments with duodenal secretion because admixture of gastric juice with duodenal secretion could not at first be satisfactorily prevented. This was finally solved by having one of the medical students swallow a balloon which was inflated as a stopper in the pylorus while duodenal juice was collected through a tube. Under these conditions, duodenal juice was found not to contain the active principle. As the result of these experiments, Castle hypothesized that Addisonian anemia was a deficiency disease of a new type caused by lack of a substance produced during the course of normal digestion. In the healthy person there is secreted by the gastric mucosa, an organic substance called, by Castle, the intrinsic factor, which is thermolabile, neither acid, pepsin nor rennin but possibly an enzyme. This reacts with a protein substance which he called the extrinsic factor which is present in beef muscle, to form a heat stable antianemic principle. Subsequently, Castle showed that a few patients with pernicious anemia failed to respond in the usual manner to the mixture of beef and gastric juice but subsequently developed a normal remission when liver extract was injected. This phenomenon was attributed to defective absorption of the antianemic principle formed by interaction of the intrinsic and the extrinsic factors in the stomach.

That the deficiency of the intrinsic factor was not an absolute one in all cases of pernicious anemia was suggested by the work of Isaacs and Goldhamer at Ann Arbor, who collected 1,500 cc. of gastric juice from 5 patients and allowed it to interact with beef. When the resulting mixture was fed to a patient with pernicious anemia it revealed that a moderate amount of the intrinsic factor had been present in the pooled gastric juice.

In tracing the development of knowledge on the etiology of pernicious anemia, it may now be pertinent to ask the question, "Where does the liver come into the picture?" This question was effectively answered by 3 groups of investigators, Wilkinson and Kline in England, Goldhamer and Isaacs at Ann Arbor, Richter, Ivy and Klim in Chicago. These investigators found that when extracts were made of human livers and injected into patients with pernicious anemia, the results were as follows:

Normal human liver: potent.
Pernicious anemia liver in relapse: impotent.
Pernicious anemia liver in remission: potent.
Cirrhosis of liver without macrocytic anemia: potent.
Cirrhosis of liver with macrocytic anemia: impotent.

These experiments indicated that the liver served as an important storehouse of the antianemic principle and that in conditions with Addisonian anemia, the liver did not contain the material in significant amounts. As a result of the investigations which have been described, it is now clear that there are 4 mechanisms by which Addisonian anemia may be caused: (a) Failure of the stomach to secrete adequate amounts of the intrinsic factor of Castle, (b) inadequate intake of the extrinsic factor of Castle, (c) failure of absorption of the antianemic principle formed by the interaction of intrinsic and extrinsic factor in the stomach, (d) failure to store the antianemic principle.

When it is said that pernicious anemia may result from failure to secrete the intrinsic factor, it is obvious that the cause of this failure is not explained. In 1933, Arthur Hurst in the Alvarez Lecture of the American Gastro-Enterological Association, offered an explanation of why the failure occurred. He pointed out that the stomachs of all individuals are constantly subjected to insults, thermal, mechanical, chemical and bacterial, but that the anatomy and physiology of the gastro-intestinal tract of 80 per cent of the population is so perfectly adjusted to the exigencies of ordinary life that they are likely to reach old age without ever suffering from any form of chronic gastric disorder as a result of these insults. Half of the remaining 20 per cent are born with a hypersthenic gastric constitution characterized by a short, high, rapidly emptying stomach, hyperchlorhydria and very little mucus secreted to protect the lining. This group is subject to the effects of autodigestion of injured mucous membrane and the formation of chronic ulcers. The other 10 per cent of the population is composed of those who have the so-called hyposthenic gastric constitution characterized by a long, low, slowly emptying stomach, and hypochlorhydria. As the result of the lowered antiseptic action of the gastric juice and a mechanism which fails to protect properly against irritants, chronic gastritis and finally achlorhydria may occur, and individuals in this group are the ones who tend to develop pernicious anemia and carcinoma of the stomach. Sixty-five per cent of cases of gastric cancer are found within this group. The remaining 35 per cent are believed to be predominantly secondary to chronic gastric ulcer. Hurst states he has never seen a case of cancer with achlorhydria in which the achlorhydria ensued after the onset of the malignancy.

The development of the concept of an antianemic factor formed by the interaction of an intrinsic and extrinsic factor in the stomach, took an unexpected turn as the result of the work of Roger Morris in 1932. He concentrated normal gastric juice by vacuum distillation to a volume of 5 to 8 cc. and after neutralization injected it into patients with pernicious anemia. This resulted in an intense reticulocyte crisis which lasted from 34 to 44 days and was accompanied by a remission of the disease. He hypothesized that the results were due to a hemopoietic hormone contained in gastric juice which he named Addisin.

In criticism of these experiments, the suggestion was offered that the gastric juice which Morris injected contained the intrinsic factor which interacted with extrinsic material in the patient's muscle at the site of injection. This argument was disposed of when it was shown by biopsy that the tissue at the site of injection was unchanged. It was then said that the gastric juice produced these striking results by means of a toxic action on the bone marrow; the fever, chills and violent systemic manifestations that followed the injection were evidences of such a harmful action. Subsequently, Fouts, Helmer and Zerfas in Indianapolis disposed of this argument by showing that when the gastric juice was concentrated by ultrafiltration at low temperatures, the systemic disturbance occurred without affecting the blood picture. When the above inactive ultrafiltrate was diluted with water and reconcentrated by vacuum distillation at 40°F., the material proved potent. Furthermore, gastric juice concentrated by ultrafiltration and stored on ice for 2 months was also found to be active. To explain these unexpected findings the authors concluded that gastric juice contained a certain amount of the extrinsic factor which interacted with the intrinsic factor under suitable conditions of time and temperature and that the injected material was merely a concentrate of the resulting antianemic principle. The question of the source of the extrinsic factor in gastric juice has not yet been satisfactorily answered. It has been suggested that it might be derived from the protein of mucin or cell debris. In this connection, it is interesting that Randolph West in New York, in fractionating liver, has derived a material which has a structure similar to the products of enzyme action on mucin.

In 1931, Reimann in Germany found that the potency of liver could be enhanced by permitting it to interact with gastric juice. Shortly thereafter, Walden and Clowes also found that when gastric tissue and liver were permitted to interact at suitable temperatures, a product resulted which was more potent than could be accounted for by the summation of the effects of the liver and gastric tissue employed. In 1933, McEllroy and Herron went a step further and demonstrated that by merely permitting autolysis to take place, the potency of liver could be increased without the presence of gastric juice or gastric tissue. They offered the hypothesis that the enhanced potency resulted from the hydrolysis of nucleoproteins by the action of nucleoproteinase during autolysis.

According to McEllroy and Herron, nucleoproteinase is an enzyme present in every cell and in normal gastric juice and may be the so-called intrinsic factor. Castle had previously tested vegetable nucleoproteins without convincing results.

While the work previously described was going on, simultaneous efforts were being made to discover the nature of the extrinsic factor. Its relation to vitamins was suggested by many provocative experiments. In 1933, Webster and Armour were able to produce complete anacidity in dogs without anorexia or inanition by diets deficient in the vitamins. They were able to restore the gastric secretion by feeding autoclaved or powdered yeast and when these were again withdrawn, the gastric anacidity was reproduced. A year later, Cowgill and Gillman reported the development of achlorhydria in dogs on a ration deficient in vitamin B. The obvious parallelism between the atrophic glossitis of pellagra which is related to deficiency of the vitamin B complex, and that of pernicious anemia, was highly suggestive. The question has arisen whether pernicious anemia may not represent more than the simple deficiency of one factor and whether the glossitis and perhaps even the central nervous system manifestations may not be due to an associated deficiency of vitamin G. Certainly there is no direct parallelism between the degree of anemia and the severity of the central nervous system symptoms and the glossitis. We have seen cases in which there were less than a million red blood cells with only minimal or scarcely detectable central nervous system manifestations and other instances in which the neurological disturbances so overshadowed the rest of the picture that the nature of the slight anemia had not been appreciated. In other instances, patients have come to the hospital complaining of sore tongue when the blood picture of pernicious anemia could only be detected by extensive hematological studies.

The question whether materials containing the vitamin B complex could serve as a source of the extrinsic factor gave rise to conflicting reports. Connery and Goldwater, and Russell reported positive results, but Strauss, Castle, Cohn and Minot could detect no response. However, Lucy Wills in India reported excellent results when autolyzed yeast was fed to patients with tropical anemia, a condition resembling pernicious anemia but with or without achlorhydria.

Strauss and Castle next incubated autolyzed yeast and an 80 per cent alcoholic extract of autolyzed yeast with normal gastric juice and obtained remissions in cases of Addisonian anemia. They concluded that the extrinsic factor was closely related to vitamin B_2, if it was not vitamin B_2 itself.

Lucy Wills, however, pointed out that an 80 per cent alcoholic extract inactivated vitamin B_2 and that egg white which is rich in vitamin B_2 when incubated with gastric juice produced no response in cases of tropical anemia and pernicious anemia. She further demonstrated that straight yeast and gastric juice were inactive, whereas autolyzed yeast under the same conditions was as potent as liver extract. As the result of these experiments, Castle retracted the suggestion that the extrinsic factor was closely related to vitamin B_2.

In a very recent paper (January, 1936) Greenspon of Montreal stated that in 1924, before the advent of Minot and Murphy's report, he had conceived a theory to explain the etiology of pernicious anemia. This theory, a hybrid of Castle's and Roger Morris' ideas, presumes that the stomach secretes a hemopoietic hormone which is destroyed by pepsin. The rôle of beef is not to serve as a source of extrinsic factor but as an agent to adsorb the pepsin so that the hormone may escape destruction and influence hematopoiesis. It fails to explain why adsorbents superior to beef, such as kaolin or aluminum hydroxide might not do the same thing and why autolyzed yeast works and straight yeast does not, or why beef is active whereas spleen is not. Experimentally, Greenspon's notions, which attracted much attention, have been refuted by Ungley and Moffett in England, and by Hanes, Hanson-Prüss, Edwards, and Castle in this country.

Massa and Zolezzi have recently attempted to revive the old theory that pernicious anemia is due to the action of toxins on the bone marrow. Utilizing the idea that the dye, Congo red, possessed certain detoxifying properties, they injected it into a number of patients with pernicious anemia and were able to report striking remissions resembling those reported by Morris after the injection of concentrated gastric juice. This work was repeated by Mermod and Dock in this country and was said to have been supported by injection into guinea pigs. However, other investigators have been unable to verify these startling observations.

Progress in the study of pernicious anemia and its treatment has been seriously handicapped by lack of a laboratory method for assaying antianemic preparations. For a number of years workers have thought that the pigeon would serve as a suitable assay animal, but the reliability of the method has never been generally accredited. In 1933, Jacobson announced that the normal guinea pig could be used to test the potency of antianemic preparations. His work received rather general recognition, but Goodman, Geiger and the author have subjected this test to a critical study over a period of 2 years and have regretfully been unable to substantiate either the theory or the usefulness of the test.

PERFORATED GASTRIC AND DUODENAL ULCERS*†

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This paper represents a brief analytical study of perforated gastric and duodenal ulcers for the last 2 years at the University Hospital, in Baltimore.

Apologies are made for the choice of this surgical topic; which, although aged and worn by the voluminous literature on the subject, still proves to be of active interest to the younger men training in abdominal surgery.

From the year 1920 until 1936 there were 106 perforated gastric and duodenal ulcers admitted to the University Hospital from among 84,835 patients. In the last 2 years, from September, 1934, to September, 1936, during my term as resident surgeon, there were 36 cases admitted. These constituted 33 per cent of the total number in the past 16 years. In the previous 2-year period there were 11 cases. Through the courtesy of the visiting staff I have had the opportunity of operating upon 21 of these cases.

Reports obtained from the surgical residents of 9 of the largest general hospitals in Baltimore summate a total of 145 perforated ulcers admitted to those institutions in this same 2-year period. From these reports it was noted that despite the larger bed capacity, fewer cases were admitted to the more private hospitals. This fact was noted in the presented 36 cases in which only 7 patients occupied private beds and 29 charity beds.

Of these 36 patients 35 were males. As compared to other reports, the incidence of colored to white was high, there being 7 colored to 28 white males. The age range was 20 to 75 years with an average age of 44 years. There was no unanimity as to the time of day that these perforations occurred. Seasonally, the greatest percentage of perforations occurred in May and June, and in September and October. Twenty-one of the cases were from the city and 15 from the state.

In attempting to explain the sudden increase in the number of perforated ulcers admitted to the University Hospital, we have considered 2 factors: first, an increase in the use of alcohol since the repeal of the Eighteenth Amendment, and second, the general economic state brought on by the depression with the consequent individual neglect of diet, oral and general hygiene, particularly in the lower strata of society.

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* Read before the joint meeting of the Baltimore City Medical Society and the Medical Society of the District of Columbia, in Washington, October 28, 1936.

† From the Department of Surgery, University of Maryland School of Medicine.

Alcohol seemed to be a negligible factor since only 5 of these 36 cases gave a positive history. The resident at the Baltimore City Hospitals reported 8 positive histories out of 20 patients in the past year. As has been stated, the incidence of perforations was higher in the lower class of patients and their mouths were greatly in need of attention. It was suggested, therefore, that the Vincent's organisms might have a direct relationship to the production of gastric ulceration. However, since these organisms are such common inhabitants of the oral cavity of so many people who do not suffer gastric disturbances and since it is unlikely that these organisms could survive the acid content of the stomach, this explanation does not seem plausible. Positive mouth cultures were obtained from several patients, but the organisms were not recovered by peritoneal culture.

In the majority of the cases the clinical diagnosis was clear-cut. The house staff became ulcer-conscious and at one period 3 cases were admitted within 4 days. The case histories were, in a number of the patients, typical and yet very interesting. One patient's ulcer perforated while he was driving a truck; he stopped and after one half hour in a cramped position drove his truck to the accident room. He was operated upon in less than 1 hour after his abdominal accident occurred. Another man's ulcer perforated while he was serving a customer in a grocery store, and after leaning with his full weight over the counter (illustrating the desire for pressure), unable to talk, pushing against the counter and sweating for some minutes, he asked to be taken to the hospital. Still another man who had received a barium meal and left a clinic suffered his perforation in the office of his employer while asking for leave of absence. Again, a patient in the county had his perforation shortly after breakfast while weeding flowers. He lay in his back yard with the watering can against his abdomen until he could call for help; 3 hours later at operation the creamed chip-beef he had eaten for breakfast was aspirated from his pelvis.

In the early cases the clinical findings were approximately the same—a normal or slow full pulse, normal or lowered temperature and leukocyte count, slightly lowered blood pressure, rapid grunting respirations, boardlike rigidity of the abdomen, disinclination for speech and resentment for the palpating hand. Seven of these patients did not give a history of previous gastric complaint, and 8 gave histories of only mild gastric disturbances for 1 year or less. Vomiting occurred in 16 of the cases. The late cases presented evidence of general peritonitis without localized tenderness, and unreliable histories were obtained from these toxic patients.

Pneumoperitoneum was diagnosed clinically and by X-ray in a number of the patients.

In the 36 cases 3 mistakes were made in diagnosis; all 3 were in negro males. In 2 appendicitis with perforation and generalized peritonitis was suspected. Reid suggests that this error is due to the shunting of the stomach contents to the pelvis by the root of the mesentery. In the third spontaneous right pneumothorax was diagnosed. This last patient was observed overnight, and an X-ray film the following morning revealed air beneath the diaphragm. He died of pneumonia 12 days after operation.

Since 1880 when Mikulicz failed in the first case ever operated upon for perforated ulcer, various surgical maneuvers have been and are constantly being suggested for the treatment of this abdominal mishap. Only one united opinion seems to exist among surgeons as to the type of operation. The opening in the stomach or bowel must be closed.

Certain authors, in the treatment of this condition, insist on one type of operation. Reviewing the late literature on the subject we find that some European surgeons recommend gastric resections even in the face of peritonitis and report a mortality rate as low as 17 per cent in a series as large as 775 cases. Others advocate simple closure of the perforation. We, however, agree with those surgeons who advise that the procedure performed is dependent on the surgical risk, the time factor, the type, size and location of the lesion. Of these 36 patients 34 were operable, the other 2 were moribund on admission and died in shock. Simple closures with omental grafts were performed in 18 cases, and of this number 3 patients so far have returned for secondary operations because of obstruction. Simple resections were done in 2 cases. Posterior gastro-enterostomy combined with simple closure and omental graft was done in most of the perforations of 8 hours or less. In this series 14 posterior gastro-enterostomies were performed in addition to simple closure at the time of operation. Graves reports 30 to 50 per cent more complete cures with this combined procedure.

The perforations were gastric in 22 cases and duodenal in 14. One of the 2 patients not operated upon showed multiple perforations of the duodenum at necropsy. There was 1 case of a second perforation. The size of the perforations varied from a large needle hole to the size of a penny.

In all cases an upper right paramedian or an upper transverse incision was made, and of the total number there was 1 fatal postoperative abdominal disruption and 3 partial disruptions, all of which recovered following secondary closure. Silk suture material was used in closure in 3 cases including the fatal one. Drainage of the abdominal cavity was instituted at operation in all but 4 patients. In practically all of the cases the peritoneal cavity was flushed with normal salt solution to remove the gross debris, following which one half to 2 liters of this fluid was poured into and allowed to remain in the abdominal cavity. Likewise, practically all of the patients received intravenous glucose and normal saline during the operation. Either spinal or general anesthesia was administered to this group.

As is generally known, the prognosis bears a direct relationship to the time elapsing between perforation and operation. If the patient is treated surgically up to 12 hours after perforation the mortality rate runs approximately 26 per cent and increases to 90 per cent after the twenty-fourth hour. In this series operations were performed as early as 40 minutes and as late as 72 hours after perforation. Five patients were operated upon after 24 hours, 3 of whom died. Of the 34 patients operated upon 8 died, a mortality rate of 23.5 per cent. The causes of death were pneumonia in 5 cases, shock in 2 and intestinal obstruction in 1 case. One operation was complicated by subphrenic abscess.

Seven of the 22 living patients have had X-ray studies made several months after operation, and from the reports it was noted that there was less deformity of the duodenal bulb in those cases in which gastro-enterostomy had been performed.

Summary

1. A brief analytical study of 36 cases of perforated gastric and duodenal ulcers is reported, representing a 2-year period at the University Hospital.

2. The incidence in this 2-year period was greatly increased over the previous one, slightly over 3 to 1.

3. Patients of the lower strata of society composed 81 per cent of the total number of patients, 19 per cent of which were colored males.

4. The average age of the patient was 44 years. The most common seasons were spring and fall.

5. Three mistakes were made in diagnosis.

6. The surgical procedures followed were simple closure with omental graft, simple closure combined with gastro-enterostomy and simple resection. Of the 34 patients operated upon, all but 4 were drained.

7. The prognosis was directly proportionate to the time elapsing between perforation and surgical intervention.

8. The mortality rate in this series was 23.5 per cent.

9. Of the 7 patients studied postoperatively by X-ray less deformity of the duodenal bulb was noted in those in which combined gastro-enterostomy had been performed.

ALCOHOL INJECTION OF LUMBAR SYMPATHETIC GANGLIA IN ARTERIOSCLEROSIS OF THE EXTREMITIES*

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During the past decade the rôle the sympathetic system plays in heat control and blood pressure has produced extensive clinical and experimental study. Out of these studies has developed more conservative methods of treatment for the various vascular disturbances of the extremities which heretofore had been relegated to the surgeon for amputation with the resulting morbidity and economic problems or, far too often, a fatal result because of the poor operating risk of this type of individual.

De Takáts states, "A systematic examination of older patients with arteriosclerosis or diabetes reveals a frequent impairment of circulation, particularly if signs of early cardiac weakness, such as a drop of the blood pressure, appear. An examination of the peripheral circulation of the diabetic or arteriosclerotic who does not have frank symptoms of vascular impairment has considerable value. It is in this stage that conservative methods may conserve the limb."

The phase of treatment which will be dealt with in this paper is especially applicable to elderly, hypertensive arteriosclerotic or diabetic individuals who are all poor surgical risks and who compose the major portion of the group suffering from painful and crippling vascular diseases. Also, this type of individual makes up a goodly portion of the static population of our institutions.

Hence, if a means of prevention of chronic vascular ulcers, arteriosclerotic and diabetic gangrene, erythromelalgia, causalgia, and intermittent claudication can be found and judiciously applied, it not only will afford great relief to the patients so affected, but will reduce the economic burden of caring for this class of individuals.

With this in mind a method of therapy is offered in the form of alcoholic ablation of the lumbar sympathetic ganglia for increasing the vascular supply to the lower limb. To better establish the rationale of this procedure, a brief résumé of the anatomy and physiology of the vasomotor apparatus is essential.

Robinson states: "The sympathetic system comprises a pair of elongated ganglionated trunks extending the entire length of the body from the base of the skull to the coccyx, connected to the peripheral spinal nerves by one series of nerves and to the visceral nerves by a second series. . . . The efferent fibers are distributed through the gray rami communicantes through the peripheral cerebrospinal nerves to the glands, blood vessels and involuntary muscles in the course of the somatic division of the spinal nerves." Whereas the cervical and thoracic portion of the sympathetic chain are not considered in this article, their anatomy will be omitted. The lumbar division of the sympathetic trunk is composed of a variable number of ganglia, usually 4, connected by an association cord, which above is a downward continuation of the thoracic trunk and below becomes the sacral portion (Frantz). In the lumbar region, the trunks tend to approach each other, with the result that they lie anterior to the bodies of the vertebrae and behind the aorta on one side, and the vena cava on the other, medial to the origins of the psoas major muscles. The branches of this subdivision are:

"1. White rami communicantes, which are received from only the first, second, and occasionally the third lumbar nerves. These fibers probably end in the sacral plexus.

2. The gray rami communicantes, which are given off to each lumbar cerebrospinal nerve. Through these nerves they are distributed to the sebaceous and sweat glands, to the smooth

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* Read before the Section on Neurology and Psychiatry of the Society, October 1, 1936.

muscles of the skin, to the blood vessels which lie in the territory supplied by the nerve in question, and also, probably, to the skeletal muscle of that same region." (Robinson)

3. Branches to the aortic plexus and the hypogastric plexus.

4. Small fibers to the vertebrae and adjacent tissues.

The method by which the sympathetic system controls the vasomotor activities is a point of dispute (Scupham and de Takáts). Wright and Duryee state: "The capillary wall is composed of an inner endothelial layer and an outer network of muscular fibers and large cells called 'Rouget cells,' " which they feel are the heart of capillary contractility. Hassin, Clark and others, however, doubt the contractile properties of the Rouget cells. Kuntz states: "That the capillary vessels are functionally innervated is generally conceded. . . . However, the data available at present do not warrant the conclusion that all capillaries are innervated." Landis, Lewis, and Krogh are of the opinion that independent contractility, without neuron control, and blood pressure are responsible for capillary fluctuations.

Hinsey, in working on the cat, found: "All postganglionic neurons giving rise to vasoconstrictor fibers to the muscles of the extremities are found in the sympathetic chain, so that removal of the lumbar sympathetic trunk should completely denervate the extremity." Ablation of the trunk by injection should do likewise.

In 1862 Secquet (Scupham and de Takáts) described a mechanism of arteriovenous aneurisms occurring normally in the skin of the fingers, hands, toes and feet, and other exposed portions of the body. "It is apparent that they must be taken into consideration in dealing with peripheral circulation in whatever area they occur because of their number and activity."

Popoff describes the entire unit of the anastomosis as a "glomus." These lie just below the subpapillary web of the skin of the hands and feet and are composed of the following parts: the efferent arteriole, the anastomotic canal (which he calls the Secquet-Hoyer canals), the neuroreticular and highly vascular tissue about the canals, the collecting venules and collagenous tissue.

The efferent artery is richly endowed with nonmyelinated fibers, and the tissue about the Secquet-Hoyer canals is of a neurovascular type.

The function of the glomus is to regulate the heat of the part. When the part is stimulated by cold the Secquet-Hoyer canals open, diverting the blood directly from the efferent arterioles to the collecting venules with much greater rapidity and volume than can be delivered by the usual capillary bed. This engorgement of the venous bed gives a great increase in surface area for heat dissipation. Likewise, the blood volume to the part is correspondingly increased.

Ranson states that these anastomoses are under the control of the vasomotor fibers of the sympathetic system.

In arteriosclerosis the pathological picture is a hyalinization of the efferent artery, but if the venous bed can be opened the rate of flow through the efferent artery will be increased even though the lumen is stationary in caliber.

With these facts before us, we may now develop the rationale for the removal of the sympathetic control in those conditions due to arteriosclerosis of the extremity. The pain, cramping, easy fatigue of the muscles, and the terminal gangrene in this condition are due to anoxemia produced by deficient blood supply (Osler, Pickering), hence if the blood supply to the part can be increased by the removal of the vasoconstrictor control, the relief of the condition is logically forthcoming.

In addition to this theoretical rationale for the procedure, Horton, by injection of mercury into amputated limbs of individuals who had previously had sympathetic denervations, found that the blood volume capacity of the denervated limb was increased to 5 times that of the undenervated limbs. Likewise, histological studies of the blood vessels of these same specimens showed an increase of vein-artery ratio in the smaller vessels from the normal 2:1 to 3.5:1 ratio in the denervated leg, thus showing graphically the effect of sympathetic ablation.

To accomplish sympathetic denervation of the lower limbs, two methods are offered, ganglionectomy, or injection of the ganglia *in situ* with novocain or alcohol.

The first, ganglionectomy, is the theoretical method of choice, but due to the fact that the procedure involves extensive surgical skill and experience on the part of the operator and severe surgical shock to the patient, which is of great consequence in dealing with the arteriosclerotic and diabetic individual, this method is not applicable to the conditions under discussion.

Injection of the ganglion, then, is the method of choice from a practical standpoint (Scupham and de Takáts, Flothow, Stern).

The diagnosis of early vascular impairment is a relatively easy procedure requiring no special equipment or apparatus other than the usual clinical tools, the sphygmomanometer, the stethoscope and the hypodermic needle.

Pickering describes 3 simple tests for vascular impairment, and de Takáts adds a fourth. These are reactive hyperemia, reaction of intermittent claudication, palpation of the pedal arteries, and cutaneous reaction to histamine. Briefly, these procedures are as follows:

Reactive Hyperemia. The examination is carried on in a warm room (70°F. to 80°F.), and the patient is given sufficient time to become acclimated. If he is cold, blankets and water bottles may be used.

Both legs are heated to 90°F.–95°F. by use of a water bath, blankets, or artificial heat, for a period of 10 minutes. The leg is then elevated above 45° for sufficient time to allow the venous tree to empty, and the circulation is abruptly stopped by inflating a sphygmomanometer cuff to a point above the foredetermined systolic pressure of the limb. The leg is then returned to the bath or pack for 4½ minutes, after which period it is removed, dried and laid horizontal in a good light, the pressure suddenly released, and the reaction observed.

When the vessels are normal the flush is even and bright and reaches the digits in 2 to 5 seconds, attaining its maximum intensity in less than 15 seconds and quickly fading.

If there is structural disease of the vessels, the flush spreads slowly and unevenly, is spotted, cyanotic in hue, and may not reach the tips of the digits for 30 to 90 seconds, and may persist several minutes.

In discussion of this reaction Pickering states: "The advantage of the reactive hyperemia is that it requires no special apparatus and is in our experience as delicate as any single test yet devised."

Reaction of Intermittent Claudication. The circulation of the limb is occluded with a sphygmomanometer and the foot is extended against resistance at the rate of one excursion a second until the pain occurs in the calf, and continued until it becomes unbearable. In the normal limb the pain usually occurs in 20 to 30 seconds, becomes unbearable in 70 to 90 seconds, and disappears in 5 seconds after release of the circulation.

In the limb with diseased vessels, if the procedure is carried out without circulatory arrest and the time of onset, unbearability and recovery are noted, it will give criteria to judge the patency of the vessels, especially when compared with the same test with the circulation arrested. Fifteen to 20 minutes should be allowed between tests, however.

Palpation of the Pedal Arteries. This procedure is a common one, and because of this the anatomy will not be here described. However, the value of this method can be greatly enhanced by warming the member in a water bath or pack prior to examination (Pickering). Reich also calls attention to the fact that, due to the wide anatomical variation in vascularization of the foot, the pulse can often be felt in other localities than the ones usually described. It has been found that this pedal pulse is absent in 5 per cent of normal individuals and misplaced in 8 per cent and that extravascular factors such as adiposity, edema, and ligamentous structures occasionally interfere. Pickering concludes: "The failure of pulsation in a warm limb is a certain sign of structural disease."

The Cutaneous Histamine Reaction (de Takáts). The skin is lightly cleansed with alcohol, care being taken not to scrub the site of injection. On the lower extremity 0.1 cc. of a 1:1000 solution of histamine* is injected intradermally on the sole of the foot, above the internal malleolus, on the middle third of the calf, above and below the knee, and on the middle third of the thigh. The resulting reaction or "flare" is recorded as "none," "faint," "fair" or "marked," at intervals of 5, 10 and 15 minutes. In the normal skin there is a marked vasodilatation or "flare" at the site of injection, due to local nervous reflex, hence the degree of reaction is an indication of the degree of arterial impairment.

In discussion of this test de Takáts states: "In a beginning arterial involvement, which is not uncommon in arteriosclerotics, delay or absence of the histamine reaction around the ankle gives an early warning. With proper prophylactic methods at this time the vascular impairment may never progress to frank gangrene."

These 4 simple diagnostic tests for vascular impairment are supplemented by many others, some involving dermatherms, thermocouples, special skin thermometers and oscillometers, but from a practical standpoint these refinements are not necessary and seldom available.

The perivertebral injection of the sympathetic ganglia for relief of pain and increasing the blood supply to the extremities is a relatively recent development. Stern in 1930, and Flothow in 1931, report it in cases of all types of vascular and neurotrophic conditions, and others report its use in angina pectoris and hypertension (Frantz). The simplest technic, however, is offered by Flothow as a modification of Lundy's technic.

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* Eli Lilly & Co. ampules.

> The patient is placed in a cool room with his extremities exposed for a period of 30 to 45 minutes. He is then placed on the table prone, and so adjusted with pillows that the lumbar curve of the spinal column is as straight as possible. Only one side is usually injected at a time, so that the opposite member can be used as a control. The field is prepared from the gluteal crease to the thoracic level, and the spines of the first, second, third and fourth lumbar vertebrae are palpated and marked. A weal of 1 per cent novocain is made 2½ to 3 cm. from the midline on a level with the interspaces.
>
> A 20- or 23-gage Labat or spinal puncture needle is inserted through each weal at right angles with the skin until the transverse process is encountered (usually 3 to 5 cm. deep). The needle points are then slipped above or below the transverse process and inserted 3 cm. further with but slight inclination of the point toward the midline. (Occasionally when the needle encounters the ganglion the patient will experience a sensation of warmth in the calf or foot. This may be utilized as a guide if it occurs.) The points of the needles now lie on a level with the anterior third of the bodies of the vertebrae and approximately 3 cm. from the midline. All 4 needles are placed prior to injecting any of them. Into each of the needles 5 cc. of 1 per cent procaine solution is injected and the reaction observed for a period of 20 to 30 minutes.
>
> If the needles have been correctly placed in about 10 to 15 minutes a flush of the injected side is noted, and as this continues (20 to 25 minutes) the leg becomes palpably warmer than the opposite one and still later the veins of the calf and dorsum of the foot will be visibly engorged. The skin will be dry and occasionally pulsations which were not palpable prior to injection can be felt. A dermatherm, thermocouple, or skin thermometer will show increase of temperature from 5°F. to 11°F. in the average case, but the use of these instruments is not essential.
>
> If the foregoing changes take place, it is assumed that the needles are placed satisfactorily, and then 5 to 7 cc. of 95 per cent alcohol is injected into each needle and the needles withdrawn.
>
> The height of the reaction is usually reached in 1 to 2 hours.
>
> The procedure is essentially painless, no preoperative sedation is necessary, and cases of operative shock have not been reported in a large series of patients.

This type of sympathetic obliteration is not limited to arteriosclerosis alone, but is employed in all vascular diseases of the extremities. Its use in Raynaud's disease, thrombo-angiitis obliterans (Buerger's disease), and diabetic gangrene, has been widely reported. Its use in cases of developed gangrene may be of value, not in preventing amputation of the part, but of insuring better blood supply to the stump and aiding in determining the level of amputation.

The duration of the denervation by this method varies greatly. This is due to the variation in the proximity of the needle and ganglion at the time of injection, a factor determining the concentration of the alcohol when it encounters the nerve tissue. Another diluting factor is the presence of the novocain solution. This can be reduced by allowing an interval of 15 to 30 minutes to elapse between the novocain and alcohol injection to insure a more complete absorption of the novocain. Flothow suggests the omission of the novocain entirely when the operator has become proficient and experienced enough in the procedure.

If the needle and ganglion are directly in contact, the ablation is a permanent affair; in others there has been a complete occurrence of the vasoconstrictor control after periods of 2 months. Flothow states: "We have noted continued vasodilation present 1 year following injection. We have also noted its disappearance within 1 month." He goes on further to state that they have reinjected cases after 5 months of relief from all symptoms and the second injection was as satisfactory as the previous one. From this and other sources, one would conclude that as a rule the procedure gives relief from the pain and promotes increased vascularity to the part on the average of about 6 to 9 months or longer, dependent upon the efficiency of the operator; and that upon the recurrence of the vasoconstriction, the pain or the other evidence of regeneration of the nervous control, a second injection will again alleviate the symptoms.

Occasionally the continued reaction is somewhat less than the immediate response and this is probably due to the greater diffusibility of the novocain as compared to that of the alcohol.

The only sequelae of the alcoholic injection is a temporary alcohol neuritis of the somatic nerves which occurs in about 50 per cent of the cases, persisting for 2 to 6 weeks, as a rule, but which is usually controlled by heat and sedation. In speaking of the untoward result Flothow states: "In the dorsal region this neuritis is often very severe and most annoying to the patient. . . . In the lumbar injections the neuritis occurs in only about one half of the cases and is usually not as severe."

ILLUSTRATIVE CASE

A case of arteriosclerotic gangrene in which lumbar injection was successful is now reported, and the like of which, it is felt, can be prevented by early institution of the suggested therapy.

C. D., a negro male, aged 57 years, was admitted to St. Elizabeths Hospital on November 14, 1931, after adjudication in the Lunacy Court of the District of Columbia. A diagnosis of alcoholic psychosis with acute hallucinosis was made.

On admission, his physical examination showed "No abnormalities of gait, skin normal, supportive system unremarkable, chest clear, blood pressure 158/90, marked thickening and tortuosity of superficial vessels and slight cardiac enlargement, a slight edema and mild varicosities of the right leg." Neurological examination was negative and the retinal vessels showed marked beading and notching of the veins. The blood Wassermann test was negative; the blood nonprotein nitrogen was 26.6, the blood uric acid 4.1, the blood sugar 94, and the blood cholesterol 222.2 mg. per 100 cc. of blood. Urinalysis was normal. A clinical diagnosis of generalized arteriosclerosis with mild hypertension was made.

He adjusted well to hospital routine, attained parole and visit status, which he satisfactorily handled, until January 28, 1933, when he received a superficial injury to the right great toe. In the ensuing month the wound failed to heal, the nail sloughed, and the bone became involved in spite of hospitalization. On March 8, 1933, the toe was amputated at the metatarsophalangeal joint. This wound failed to heal. The metatarsal bones became infected and sequestrated, and in October, 1933, the patient was sent to the chronic hospital service.

A year later, October 10, 1934, the patient developed increased drainage from the site of the old wound; the foot became cold and black. A week later he was hospitalized again, and on November 17 the right leg was amputated at mid-thigh. The postoperative course was uneventful.

On June 17, 1935, the patient developed aphasia and complete paralysis of the left side of the body. His blood pressure was 170 systolic and 85 diastolic and his blood chemistry was within normal limits. A diagnosis of cerebral thrombosis, right, was made. After 10 days, he recovered the use of his left arm and his speech, but his leg remained paralyzed.

On December 1, 1935, the patient developed a suppurative process between the first and second toes of his left foot. This did not respond to treatment, the toes became necrotic, and on admission to the hospital, December 3, there was a definite line of demarcation at mid-foot. The drainage was profuse and the leg painful.

On January 4, 1936, an alcoholic injection of the left lumbar ganglia was performed by the described method, not with the hope of improving the gangrenous foot, but to improve the vascularity of the leg to insure healing of the stump. Fifteen minutes after injection, the leg was palpably warmer, the veins engorged, and the patient's pain relieved. The general condition of the patient improved, the progress of the gangrenous process was retarded, and on January 20 the leg was amputated at mid-thigh.

Pathological examination of the leg showed a distinct change in the color and consistency of the muscles in the lower third of the calf, and a complete obliteration of the posterior tibial artery.

The postoperative course was uneventful, the stump healing without suppuration.

On September 12, 1936, about 9 months after the injection, the skin of the injected stump was palpably warmer and dryer than the opposite one, proving the absence of regeneration of the sympathetic control during this period.

SUMMARY AND CONCLUSIONS

1. A prophylactic measure for the care of the arteriosclerotic lower extremity with trophic changes or pain is offered in the form of alcoholic injection of the lumbar sympathetic ganglia, thereby increasing the vascularization of the part, relieving the pain of causalgia, erythromelalgia, and intermittent claudication, and reducing the incidence of gangrene with its morbidity and economic problems.

2. A brief résumé of the physiology and anatomy of the neurovascular system is given to better illustrate the rationale of the procedure.

3. Four simple, efficient tests are described for diagnosis of vascular impairment of the extremities. These are the reactive hyperemia test, the reaction of intermittent claudication, palpation of the pedal pulse, and the cutaneous histamine reaction.

4. A technic of injection of the lumbar sympathetic chain is described.

5. A case of arteriosclerotic gangrene, necessitating bilateral amputation, in which unilateral lumbar injection was successfully performed, is presented, the evidence of complete denervation being present 9 months after injection.

6. Alcoholic injection of the lumbar sympathetic ganglia is a simple, effective procedure unaccompanied by morbidity or mortality, which is applicable to senile and arteriosclerotic patients for relief of painful vascular conditions of the lower limbs, and appreciably reduces the incidence of gangrene and amputation in these individuals.

7. A judicious application of this procedure

in early cases of this type not only prevents suffering, but reduces the economic burden of caring for this type of patient, both in institutions and out.

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Decortication of the Lung for Tuberculous Pleurisy. Man, aged 44, laborer. Admitted to the Royal Hospital, Wolverhampton, complaining of pain in the left side of the chest and of cough. He brought up a little sputum and felt generally weak; he was slightly dyspnoeic while lying in bed but was not cyanosed. Temperature 99.8°F., pulse 120; respirations 28. There was very little movement of the left side of the chest, which was dull to percussion, at the apex and "stony" dull at the base.

18.8.35: 120 cc. of clear fluid aspirated from the left pleural cavity. The fluid was sterile and was negative to guinea-pig inoculation.

Repeated aspirations of the fluid were carried out but the pleural cavity rapidly refilled after each occasion. . . . Bronchoscopy showed no evidence of bronchial obstruction.

7.1.36 (Operation): A left thoracotomy was performed through the seventh intercostal space, with a view to decortication of the lung. Both the parietal and visceral pleurae were between $\frac{1}{8}$ in. and $\frac{1}{4}$ in. in thickness, and were opaque, white, glistening, tough membranes. There was about a cupful of fibrinous exudate loosely adherent to the diaphragm.

The visceral pleura was excised from the base to the apex of the lung. The separation was performed without much difficulty, except at the mediastinal surface where complete stripping was not possible. In one place the lung was slightly injured, with escape of a little air. As the pleura was stripped off the lung expanded and, at the end of the operation, about half filled the chest cavity. The opening in the chest wall was completely closed by suture.

Microscopic sections of the thickened pleura showed evidence of tuberculous infection.

The left chest was aspirated on 5 occasions between January 10 and January 17. At first the fluid was heavily blood-stained and was sterile on culture, but later became purulent. The later cultures showed staphylococci.

The wound became infected, and healing was not complete until about 3 months after the operation. Skiagrams taken at this time showed the lung to be completely expanded.

17.3.36: There was a slight rise in temperature, and 2 weeks later X-rays showed fluid in the right pleural cavity which was aspirated, 16 ounces of clear, sterile fluid being withdrawn. Following this the signs on the right side cleared up.

The patient left hospital on April 12, 1936, and has continued to make satisfactory progress. . . .

Extract from case report by R. Milnes Walker, F.R.C.S., *Proceedings of the Royal Society of Medicine, December, 1936,* p. 168.

GONOCOCCEMIA WITH ENDOCARDITIS AND RECOVERY

REPORT OF A CASE

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Cases of gonococcal bacteremia and gonococcal endocarditis have been reported in the literature for the past 80 years (Prendergast). Recovery in a proven case with or without cardiac involvement is of sufficient rarity to warrant recording. The disease most commonly occurs between the ages of 20 and 40 years and usually with some other gonorrheal complication, such as epididymitis or arthritis. I wish here to present a detailed description of a case of proven gonorrheal sepsis with cardiac involvement and recovery under observation for a year, and to comment briefly on the treatment of this disease.

Report of Case

P. G., a man, aged 34 years, was first seen at his home on March 22, 1935, complaining of painful joints, malaise, fever, inflamed eyes and urethral discharge. He stated that he had been confined to bed for 4 weeks before this visit under the care of his family physician and had had some rheumatism in his knees and ankles several days before going to bed. The illness had begun with pain in the left heel, concerning which he neglected to consult a physician. Then, about a week later he developed a morning urethral drip for which he sought medical aid. Several days later he noticed that both eyes were red, painful, and had a slight discharge. Treatment was instituted, and the patient felt able to return to work for a few days. Then the left foot and ankle became red and swollen and he was unable to walk. He was put to bed and told that he had gonorrheal rheumatism and gonorrheal infection in his eyes. The joint involvement migrated to the right foot and ankle, the right knee, and then the left knee with a definite increase in constitutional symptoms. During this time the patient was receiving internal medication and home irrigations for the urethritis, and drops for his eyes, which seemed to help these conditions considerably. The arthritis continued to become more troublesome, and the patient began to have profuse sweats with marked weakness.

At this time the attending physician became ill and I was called in to see the patient. I learned that he had had gonorrhea 2 years before with recovery. At that time he had had some arthritis which lasted about a week and did not confine him to bed. He denied recent venereal infection.

When seen at home the patient was lying in bed, pale and acutely ill, with a temperature of 100°F., and sweating profusely. The blood presure was 112 systolic and 72 diastolic; the pulse rate 100 per minute. Both conjunctivae were red and swollen but showed no appreciable discharge. Examination of the mouth revealed many filled teeth, some bridge work and cryptic tonsils. The lungs were clear, and the heart was not enlarged upon percussion. There was a very soft systolic murmur heard over the apex of the heart. A definite purulent urethral discharge was present which gave positive smears for gonococci. Several blisters were noted on glans penis, which the patient claimed were due to the solution ordered for irrigations. Both knees were swollen, red, hot and extremely painful on passive motion. Voluntary movements were practically impossible. The left knee presented evidence of fluid beneath the patella. Both feet and ankles were swollen, red, hot, and painful.

The patient was visited again on the following day, and the following changes were noted. The arthritis had migrated to the right metatarsophalangeal joint of the thumb. The general symptoms were decidedly worse, and the patient was extremely weak and unable to get out of bed. A small petechial hemorrhage was found in the gum over the upper left canine tooth, and several smaller ones were present over the shoulders. There were also some small subcutaneous nodules on the ball of the left foot at the base of the toes. The preliminary diagnosis was gonorrheal septicemia. Dr. Harry F. Dowling was called in consultation and concurred in the diagnosis.

The patient entered the George Washington University Hospital on March 28, 1935. Upon admission to the hospital his temperature was 100°F., and pulse rate was 100 per minute. The hemoglobin was 70 per cent (Dare method); the red blood cells numbered 3,860,000 and the white blood cells 12,200 per 100 cc. of blood, with 71 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes and 4 per cent eosinophiles. The blood pressure was 108 systolic and 80 diastolic. Examination of a urine specimen collected in three separate glasses showed pus, red cells, and albumin in each portion. A blood culture* showed the presence of gonococci. The blood Wassermann was negative. The patient continued to run an irregular, septic type of temperature, complained bitterly of pain in both knees and weakness, and was sweating excessively at times with preceding chilly sensations.

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* *Technic used in culturing gonococci from the blood stream.* Ten cc. of blood was collected in 50 cc. of 1 per cent calcium carbonate broth containing 1 per cent glucose and 1 per cent peptone. This was later subcultured to blood broth and blood agar plates enriched with hydrocele fluid. The organisms obtained from these growths were differentiated by the following sugar reactions: (1) Fermentation of glucose with the formation of acid, (2) no acid formed in maltose and saccharose. This reaction identified the organism as the gonococcus, rather than one of the other members of the Neisseria group.

On April 7, 10 days after admission, the patient developed a generalized rash which was found mostly over chest and back, less on the abdomen and extremities, and none on the face. Also a new petechial hemorrhage was noted over the upper sternum, and the spleen was felt 2 finger-breadths below the costal margin. Dr. Dowling was of the opinion that this rash was a drug rash as a result of the salicylates given for the relief of the arthritis. The treatment had consisted of general supportive measures, salicylates for the joint pain, urinary antiseptics, 3 transfusions of whole citrated blood, and intradermal injections of gonococcus filtrate (Corbus-Ferry).

On April 20, 23 days after admission, examination of the heart revealed for the first time a very definite diastolic murmur, heard best in the second interspace just to the left of the sternum. The systolic murmur previously noted at the apex was very faint. Dr. R. Massie Page was called in consultation at the request of the patient's family. He, too, concurred in the diagnosis of gonorrheal sepsis with endocarditis and gave a very unfavorable prognosis.

After 29 days of hospitalization and the fourth blood transfusion, the patient was allowed to go home in an ambulance. He continued to improve, became afebrile, and after about 3 weeks was able to be up and around with very little discomfort. His chief difficulty at this time seemed to be pronounced muscular weakness of both lower extremities, with some stiffness of the left knee. He appeared in my office at irregular intervals for physical checkups, and the last examination was made on March 5, 1936, about 1 year after the beginning of his illness. At this time he had gained about 20 pounds; he felt very well, and all muscular weakness of the lower extremities was gone. The same diastolic murmur in the second left interspace to the left of the sternum was present. The blood pressure was 120 systolic and 78 diastolic. The pulse rate 88 per minute.

COMMENT

Newman, writing on the prognosis in gonorrheal endocarditis, credits Ricord as the first one to report this form of heart involvement, in 1838; Brandes as the first to demonstrate clinically gonorrheal heart disease with recovery in 1854; and Hewes, in 1894, as first to recover the organism from a blood culture. Since then, reports of gonococcemia have been many. Thayer reviewed the literature in 1922 from the standpoint of cardiac complications, reporting 72 cases, including 12 new ones of his own.

Later on, in 1932, Hoffman and Taggart made a summary of the literature and reported a case of gonorrheal endocarditis. They stated that since Thayer's review 19 cases had been reported but that only 9 cases were acceptable as certain gonorrheal endocarditis. Solomon and his associates have discussed the methods of diagnosis of gonorrheal endocarditis.

The number of cases with cardiac involvement and recovery reported is decidedly small. Perry reported 1 in 1930 and later in 1933 gave further notes on this same case. Newman reported a case in 1933. Friedberg in 1934 reported 4 cases of gonorrheal sepsis with recovery, 1 of which had cardiac involvement. These cases were observed over a period of a year. Other cases without cardiac lesions have been reported as recovered by Jenkins, Cabot, O'Brien and Bancker, Wheeler and Cornell, Garlock, Filler, Rubenstone and Israel, and others.

In the present case some of the features worthy of mention are the bilateral conjunctivitis, the petechial hemorrhages, the painful plantar nodules, and the maculopapular eruption. The positive blood culture, the development of the heart murmur during the course of the illness, the splenic enlargement, and the urinary findings were all evidences of the sepsis present.

The systolic murmur which was heard over the apex during the early stages of the disease and which later began to disappear may be explained as suggested by other observers on the basis of an edema of the valves, rather than to a definite disease process. This idea was supported by the disappearance of the murmur after recovery. The development later of the permanent diastolic murmur is probably due to endocarditis of the pulmonary valve, but aortic involvement must be kept in mind.

In regard to the treatment of this disease, it is felt that strict conservatism is the rule in the care of the local infection. This was followed in this case, using only urinary antiseptics by mouth for the urethritis. In the absence of specific sera blood transfusions still remain the "sheet anchor" for the treatment of the sepsis. This patient received 4 blood transfusions. Stock vaccines, autogenous vaccines, and convalescent serum have been used with little or no success, although it is believed that vaccines do have some part in the relief of the arthritis. Favorable results have been reported from the use of intravenous iodine solution, particularly for the arthritis.

In this case, besides the means mentioned above, the gonococcus filtrate (Corbus-Ferry) was used, beginning with 0.1 cc. intradermally and increasing 0.05 cc. every 5 days up to the maximum dose used, which was 0.3 cc. (Corbus, and Cumming and Burhans). No results were noted until the dose was 0.25 cc. and the area of erythema at the site of injection was 2.5 inches in diameter. After this dose the patient would complain of an increase in joint pains and malaise for a day following the injection, but he always felt better on the succeeding day. He received 8 intradermal injections. Whether or not the use of the gonococcus filtrate played any part in the successful outcome of this case is problematical. Judging from the constitutional reactions which followed injections of 0.25 cc. or more I feel that it was of some value. However, it might be of some interest to mention that at no time during his illness in the hospital were negative urethral smears obtained. These remained positive for several weeks after the patient was sent home from the hospital.

SUMMARY

A case of proven gonococcemia with endocarditis and clinical recovery under observation for 1 year is reported. In addition to routine supportive measures and several blood transfusions the gonococcus antigen (Corbus-Ferry) was used in the treatment of this patient.

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ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"RECENT CASES OF ISTHMUS STENOSIS (COARCTATION) OF THE AORTA,"* **John T. King, M.D.**, Baltimore, Md.

Stenosis of the aortic isthmus (coarctation) can be found at necropsy in approximately 1 of every 1,500 individuals. The type of narrowing may be fusiform, involving the entire isthmus of the aorta, that portion which lies between the left subclavian artery and the point of entrance of the ductus arteriosus botalli; or it may be a sharp constriction amounting to complete obliteration near the entrance of the ductus. The two varieties are indistinguishable on clinical grounds. The diffuse type doubtless represents the persistence of the embryonic variety of isthmus, a section of the aorta which has comparatively little prenatal function. The localized type seems occasionally to occur as part of a true congenital anomaly. However, it rarely if ever can be demonstrated in embryo, and the location of the constriction lends weight to the theory that it is due to an extension of the tissue of the ductus arteriosus into the wall of the aorta, this tissue undergoing atrophy shortly after birth. The writer believes this the most likely cause of cases of complete or sharply localized constriction.

Several unreported cases illustrate certain features of the condition.

Case 1: A medical student with signs of obvious aortic and mitral insufficiency had been kept in bed for months for supposed rheumatic heart disease. There was cardiac hypertrophy; but in addition to these findings, large pulsating vessels were found along the inner margins of the scapulae, and smaller horizontally placed vessels were felt below the angles of the scapulae. There was marked exaggeration of arterial pulsation in the upper extremities, marked reduction in the legs and abdominal aorta. X-ray of the chest revealed an aortic knuckle and notching of the lower borders of the ribs. Blood pressure: right arm 210/106; left arm, 178/90; right leg, 130/125; left leg, 140/126.

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* Presented at the joint meeting of the Baltimore City Medical Society and the Medical Society of the District of Columbia, in Washington, October 28, 1936.

Case 2: A girl, aged 18 years, had no cardiovascular complaints except occasional cardiac palpitation. The blood pressure in the arms was 180 to 200 systolic and 105 to 130 diastolic. It could not be determined in the legs. Typical pulsations were present in the interscapular region. Even at the age of 18 the ribs were already notched. A lateral x-ray film showed a defect in the upper thoracic aorta.

Case 3: A young woman was suspected of toxemia of pregnancy. There was marked difference in pulsation and pressure between the arms and legs and collateral pulsations in the interscapular regions. Labor was uneventful. X-ray films showed normal heart, small aorta and notching of the ribs.

Case 4: A young woman was admitted to the Johns Hopkins Hospital for hypertension, having been refused insurance. The signs were essentially the same as in the preceding cases. The blood pressure in the arms was 180/100 and in the right leg, 112/98. The cardiovascular silhouette showed only slight reduction of prominence of the aortic knuckle, and notching of the ribs.

Case 5: A 15-year old boy showed signs of collateral circulation in the interscapular region. Blood pressure: right arm, 160/80; left arm, 134/84; left leg, 100/70 (?). The cardiac contour in a roentgenogram was essentially normal, with some reduction in prominence of the aortic knuckle. Erosions of the ribs were already beginning to appear.

Case 6: A young married woman had pulsating collateral vessels in the interscapular region. There was an intense systolic murmur in the left interscapular region transmitted to the front. Moderate exaggeration of pulse in the upper extremities with reduction in the lower was noted. Blood pressure: right arm, 122/60; left arm, 120/60; left popliteal, 108/90; right popliteal, 104/90. Other reported cases have had arm pressures within normal limits, but this occurred in only 1 arm or was determined in only 1 arm. Our patient was the only one with characteristic signs of coarctation in whom the blood pressure was determined to be normal in both arms. In spite of this there is the usual definite comparative reduction of pressure in the legs.

Because of the danger of rupture of the root of the aorta, these patients should not undertake vigorous exertion at any time, although they often tolerate it well. Even labor may be tolerated, but it is generally inadvisable. Implantation of the Streptococcus viridans on the anomaly may also cause death. With this in mind, scrupulous care should be taken to eliminate foci of infection where this organism is prevalent, especially about teeth, tonsils, and sinuses. With proper care and good fortune, these patients may attain old age.

Transfusion Syphilis. The following case is reported because it indicates that syphilis can be transmitted by blood transfusion even though the donor has a negative Wassermann test and has previously received 6 intravenous injections of an arsenical preparation.

Mrs. A. G. had received prenatal care at the Metropolitan Hospital Prenatal Clinic, where her Wassermann test was found to be negative. . . . The Kahn test on her blood was negative. . . .

. . . a transfusion of 350 cc. of blood was given, the donor being a friend of the family, S. C. No record has yet been found of a Wassermann test having been done at the X— Hospital on this donor before the transfusion was performed. His Wassermann reaction was reported by the Department of Health on September 28, 1935, as plus-minus, and on October 9 was negative.

On January 28, 4 months after the transfusion, Mrs. A. G. entered the Mount Sinai Hospital because of pain and tenderness in the lower cervical and dorsal regions in the back which she had had for about a week. Examination revealed a generalized lymphadenopathy and a palpable spleen. The blood Wassermann was 4 plus and the Kahn test on the blood 2 plus. . . . X-ray of the spine was negative. A biopsy of a supraclavicular node was reported showing inflammatory hyperplasia.

Because of the strongly positive Wassermann reaction, it was suspected that the general lymphnode enlargement might be due to syphilis. The patient was therefore given a provocative injection of neoarsphenamine 0.2 grams on February 8. Two days following the injection, she developed a typical copper-colored macular eruption on the trunk and upper extremities which was diagnosed by Dr. I. Rosen, chief dermatologist of the hospital, and Dr. L. Chargin, as a secondary syphilitic eruption. The rash gradually faded in the course of the next 4 days. Antiluetic treatment was given. The patient received both neoarsphenamine and bismuth. . . .

This case of transfusion syphilis is reported because of its unusual importance. The donor's blood was still infectious in spite of the fact that he had 6 previous injections of an arsenical preparation. He was in the primary stage of syphilis and his blood Wassermann was plus-minus on the day before the transfusion and was reported as negative 11 days after the transfusion.

The experience demonstrates that a negative Wassermann reaction on a blood donor is not sufficient to eliminate the possibility of active syphilis and of a spirochetal bacteriemia. In addition to the Wassermann test, the donor should be asked concerning syphilitic infections.

Extract from case report by Morton W. Willis, M.D., New York City, *New York State Journal of Medicine, January 1, 1937*, p. 60.

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CHEMOTHERAPY OF STREPTOCOCCIC INFECTIONS BY PRONTOSIL AND PRONTYLIN

The attempts at chemotherapy of bacterial infections have been so unsuccessful that announcement of a new chemotherapeutic agent is apt to be received with scepticism. Such a substance is Prontosil. This substance was first demonstrated to have an antistreptococcal activity by Domagk,[1] in 1935, who had been experimenting with the effect of various azo dyes on streptococcus infections in mice. He found that linkage of the dye with a sulphonamide group gave successful results in most of his experimental animals. Numerous clinical reports appeared soon thereafter in the German literature but were for the most part more enthusiastic than scientific. The first article to appear in the English literature, by Colebrook and Kenny,[2] was a report on the use of Prontosil in 38 cases of puerperal fever with satisfactory results. A number of other careful studies have subsequently appeared in English.

Prontosil is 4 sulphamido-phenyl-2 azo-7 acetylamino-1 hydroxynaphthalene-3, 6 disulphonic acid. It is employed in the form of the disodium salt in a 2.5 per cent aqueous solution, and is given intramuscularly. Its action apparently depends upon the fact that in the body it is broken down into p-aminophenylsulphonamide. The latter substance is effective when administered orally, and marketed under the name of Prontylin. In laboratory animals these substances have proven very effective in providing protection from several hundred times a lethal dose of virulent streptococci. Such protection is provided both by oral administration and intramuscular injections. These findings have been confirmed by many workers. Effectiveness against organisms other than the hemolytic streptococci has not been demonstrated, except possibly against meningococci where apparently it was of value in protecting mice. This phase needs further confirmation. It has not been possible to demonstrate protection against Streptococcus viridans, staphylococci, or pneumococci.

Clinically it has been demonstrated that the blood of patients receiving Prontosil or Prontylin is not only bacteriostatic but bactericidal. This has proven true not only in patients with Streptococcus hemolyticus infections but also in normal persons. This action is greatly in excess of anything encountered in normal blood or serum. The best clinical study on the use of this substance in the English literature is that of Colebrook and Kenny[3] who recently reported its use in 64 cases of puerperal infections due to hemolytic streptococci. This study included 38 cases which they had previously reported. The first 10 cases of the series were selected for treatment with Prontosil because of their severity. The remaining 54 were consecutive admissions treated without regard to their severity. In these 64 cases treated with Prontosil there were 3 deaths, or a mortality of 4.7 per cent. In 1935, 90 cases had been treated by them by old methods with 22 deaths, or a mortality of 24.4 per cent. In 1934, 120 cases had been treated with 20 deaths, or 16.6 per cent mortality. In 1933 the death rate had been 20.6 per cent; in 1932, 21 per cent; and in 1931, 31.6 per cent. Even taking into account the possibility of decreased virulence of the infecting organism and the possibility of a larger proportion than usual of mild cases, it would seem that Prontosil should receive some credit for this reduction in mortality. In evaluating the results of Prontosil therapy in other probably related infections, such as erysipelas and scarlet fever, the well-known tendency of these conditions to spontaneous remissions should be borne in mind.

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[1] DOMAGK, G.: Ein Beitrag zur Chemotherapie der bakteriellen Infektionen. Deutsche med. Wchnschr., 1935, **61**, 250.

[2] COLEBROOK, L., AND KENNY, M.: Treatment of Human Puerperal Infections, and of Experimental Infections in Mice, with Prontosil. Lancet, 1936, **1**, 1,279.

[3] COLEBROOK, L., AND KENNY, M.: Treatment with Prontosil of Puerperal Infections Due to Hemolytic Streptococci. Lancet, 1936, **2**, 1,319.

It should be clearly understood that our knowledge of these substances is as yet very incomplete and there is much yet to be learned concerning their use both from the clinical and scientific standpoints. The dosage is as yet not fully determined. For the more severe cases 5 to 10 cc. of the Prontosil solution is advised intramuscularly every 4 hours during the day and night. As improvement occurs the dose is gradually decreased or the patient is changed to Prontylin tablets by oral administration. Even in this dosage, however, a mildly irritant effect upon the urinary tract tissues has been demonstrated. The most striking toxic manifestation has been the development of sulphemoglobinemia in 3 cases. This was probably due to a reaction between the Prontosil and magnesium sulphate which was being simultaneously administered. This possibility should be borne in mind when Prontosil is being used. No other irritant effects have been demonstrated following the intramuscular injections. The intravenous injection of Prontosil is frequently followed by unpleasant reactions and offers no advantage over intramuscular administration. During the use of Prontosil the urine is usually stained red and there is occasionally a reddish tint to the skin.

Experimentally prophylaxis of streptococcic infections by the use of Prontosil has been demonstrated. Its use in this respect and for other types of infection must await future investigation. For the present its use should be restricted so far as possible to Streptococcus hemolyticus infections alone since this is its only proven field of usefulness.

J. R. C.

CONSULTATION IN TUBERCULOSIS

No one can know everything. This is peculiarly true in the practice of medicine. Our collective knowledge in medicine has been enormously extended. More is known today than ever before about anatomy, physiology, etiology, pathology, technic and methods in diagnosis and therapeutics. The development of specialists in the pure sciences as well as in the applied sciences is an expression of the vastness of the field of medicine itself, as also of its intensification in the various branches. Obviously, it is quite beyond any one person's ability to be master of the entire domain encompassed by present-day medicine.

Since it is so impossible for any one of us to be equally competent in all the branches of medicine, it is no reflection upon the practitioner's ability when he admits his limitations and seeks the advice of his colleagues in consultation. Quite the contrary—it is to the physician's credit, and certainly to the advantage of his patient, when the physician seeks advice and counsel. As the Arabic proverb has it, "It is a wise man who knows when he does not know."

Quite apart from the limitation which the vastness of accumulated knowledge in the field of medicine with its related sciences imposes, there is yet another reason that should prompt us to employ consultation. This particular reason concerns itself with the personality, or rather with the natural endowments of the physician, and the physician should be first to recognize its importance. The Fates do not bestow their gifts equally on all men. The gift of a retentive memory, unfortunately, is not the sole requisite of the competent physician. The medical student's letter-perfect text-book recitation does not, as is well known, guarantee an equally competent practitioner. Mechanical ability may make a clever operator, but it does not make the real surgeon who not only knows when to resort to surgical methods but who also knows when not to operate.

In spite of all the valuable laboratory and other technical methods that are available to assist the physician in diagnosis, the practice of medicine still remains an art, an art that yet depends, and likely always will, upon certain inborn qualities of the practitioner. Some have these qualities in a greater degree than others.

The powers of observation vary in individuals; the ability to draw conclusions and decide upon purposeful action likewise varies. Symptomatology, unfortunately, does not always present itself with classic text-book clearness, nor does a recognized form of treatment fit every patient.

Experience is a great teacher, but to profit from experience requires certain mental and emotional equipment and attitudes. These, too are not alike in all men. Consequently we do not equally profit from the opportunity which experience may provide.

If our profession is to maintain the position to which we believe it to be entitled, and above all, if our patients, whose health and lives are entrusted into our hands, are to have the full benefit of what medicine can give, we must consult more often. The best men in the profession, whether in general practice or in the specialities, do not hesitate to seek the counsel of their colleagues. If each of us could be big enough to recognize his limitations and to request consultative aid when those limitations have been exceeded, better medicine would be practiced, the practitioner would be wiser, and his patients would feel more than ever that they were in safe hands.

Our Health Officer, Dr. George C. Ruhland, is attempting to decrease the morbidity and mortality from pulmonary tuberculosis. He has taken physicians on his staff who have had special training in this field. These men are available as consultants, gratuitously and otherwise, depending upon the economic status of the patient. Tuberculosis is a speciality, and the handling of every case should be directed by a specialist. If the practitioner who has first contact with the case does not have any particular consultant in mind, let him not forget that Dr. Ruhland's assistants are always available.

TRANSACTIONS OF THE SOCIETY

Stated Meeting, January 6, 1937

The following were duly elected to membership:

Active Members

Theodore Judson Abernethy, 1411 Twentieth Street, N. W.
Francis Charles Allman, 127 Twelfth Street, S. E.
Abe Blajwas, 2310 Connecticut Avenue, N. W.
John Leland Cardwell, 1371 Kalmia Road, N. W.
John Warren Casady, 5022 Reno Road, N. W.
Leah Huntley Cate, 2737 Macomb Street, N. W.
Austin Brockenbrough Chinn, 1746 K Street, N. W.
Emmett Grayson Coiner, 2700 Connecticut Avenue, N. W.
Karl Coates Corley, 3921 Ingomar Street, N. W.
Allen Slayman Cross, 700 East Capitol Street
Edgar Willingham Davis, 1150 Connecticut Avenue, N. W.
John Vincent Dolan, 3100 Connecticut Avenue, N. W.
Harry Samuel Douglas, 1673 Columbia Road, N. W.
James Albert Dusbabek, 1801 Eye Street, N. W.
Thomas Aloysius Egan, 1835 Eye Street, N. W.
Martha May Eliot, 1815 Forty-fifth Street, N. W.
Clayton Bernard Ethridge, 1801 Eye Street, N. W.
John Francis Finnegan, 1342 East Capitol Street
Irvin Hantman, 1608 Massachusetts Avenue, S. E.
Russell Kuhner Hollingsworth, 1418 Good Hope Road, S. E.
Edward Lee Howes, 4622 Langdrum Lane, Chevy Chase, Md.
Helen Gladys Kain, 1801 Eye Street, N. W.
Howard Katzman, 2701 Connecticut Avenue, N. W.
Raymond Charles Kirchner, 3300 Sixteenth Street, N. W.
Edward A. Krause, 1801 Eye Street, N. W.
Leslie Keith MacClatchie, 1911 R Street, N. W.
Benjamin Manchester, 1701 Varnum Street, N. W.
Franklin Hervey Maury, 1610 Eye Street, N. W.
William Sterling Miller, 1131 West Virginia Avenue, N. E.
Charles Aloysius Millwater, 1864 Wyoming Avenue, N. W.
Leland Conner Moss, 1710 Rhode Island Avenue, N. W.
Joel Norton Novick, 1726 Eye Street, N. W.
Morris Silverman, West Clifton Terrace Apartment
Ashby Wade Smith, 2100 N. Capitol Street
Luther Henry Snyder, 5124 Chevy Chase Parkway
Maurice van Kinsbergen, 1800 Connecticut Avenue, N. W.

Associate Members

Eloise Blaine Cram, Ph.D., National Institute of Health
Jay Louis Hoffman, Saint Elizabeths Hospital
William R. Osgood, Ph.D., 3633 Ingomar Place, N.W.
Manson Bowers Pettit, Saint Elizabeths Hospital
Edward William Wallace, Ballston, Va.

Change of Membership Status

Active to Associate

Lauretta E. Kress
A. W. Truman

Applicants for membership to be voted on in March, 1937:

For Active Membership

Louis Bernard Bachrach, George Washington University—1929
Hugh Osgood House, George Washington University—1928
Robert Sterling McGrath, Tulane University—1933
Spencer Vincent Meade, George Washington University—1930
Stephen William Nealon, Jr., Georgetown University—1933
John Raymond Raedy, Georgetown University—1932
Duane Case Richtmeyer, George Washington University—1932
Alfred Henry Richwine, George Washington University—1933
Francis Thomas Sharpe, Georgetown University—1932

For Associate Membership

Alonzo Ray Dawson, Medical College of Virginia—1929
George Brackett Dowling, George Washington University—1917
David Vincent McCauley, Ph.D., Woodstock College—1928
Othmar Solnitzky, George Washington University—1920
Genevieve Margaret Stewart, Woman's Medical College of Pennsylvania—1933

Dropped, pursuant to provisions of Chapter IV, Article V, of the Constitution:

Active Members	*Associate Members*
Virginius Dabney	Viola Russell Anderson
*Charles J. Demas	Clifford G. Hines
George H. Magee	
Richard M. Rosenberg	

* Request for reinstatement pending.

Group Hospitalization, Inc.

Representatives

Pursuant to resolution adopted by the Society January 17, 1934, the following were duly nominated by the President, Dr. W. M. Sprigg, and elected by the Society:

W. M. Ballinger
Joseph B. Bogan
Caryl Burbank
Tomas Cajigas
William W. Chase
Arthur C. Christie
C. W. Culver
William T. Gill, Jr.
R. Arthur Hooe
LeRoy W. Hyde
Richard A. Kearny
Leon A. Martel
Russell McNitt
Albert E. Pagan
Philip O. Pelland
Alec A. Preece
F. A. Reuter
J. R. Verbrycke, Jr.

Central Admitting Bureau for Hospitals

Representatives

The following members were nominated to represent the Medical Society of the District of Columbia on the Board of Directors of the Central Admitting Bureau for Hospitals for the year 1937:

J. R. Verbrycke, Jr.
Henry C. Macatee
Oscar B. Hunter
Arthur C. Christie
Sterling Ruffin
Harry S. Bernton
Margaret M. Nicholson
James Alexander Lyon

Amendment to the Constitution Adopted

Chapter VII, Article III, Section 1, pertaining to the duties of the Executive Committee:

Add at the end of Section 1, the following:

No provision of this section shall be construed to grant authority to Executive Committee to commit the Society on any question of public policy; action on such matters shall always be in accordance with the provisions of Chapter III, Article II, of the Constitution.

Eight Physicians Obtain Life Membership

Through a constitutional provision members of the Society on the active roster for 40 years become life members, and are no longer liable for dues or assessments. In January of each year the Annals prints additions to this Honor Roll. In the following tabulation the seniority number and date of entrance to membership are given:

191	Jesse Shoup	April 15, 1896
193	Virgil B. Jackson	April 20, 1896
194	John Daniel Thomas	April 24, 1896
195	Phebe Russell Norris	April 28, 1896
197	Walter Augustine Wells	May 1, 1896
199	Francis Randall Hagner	May 8, 1896
200	Clarence Arlington Weaver	May, 1896
209	Edward F. Pickford	November 4, 1896

These physicians are warmly congratulated and the hope is expressed that they will be on the rolls for many subsequent years.

Forty years of continuous active membership has now brought to 51 of our esteemed fellow-practitioners release from the obligation of paying dues and assessments. They are life members. From the correspondence received we select and print the following because each letter is stimulative and helpful, especially to the younger member who now considers that completion of almost a half century of continuous membership is far, far removed in the distant future period. He personally would give this honor scant thought.

"January 9, 1937.
Dear Dr. Conklin:

I thank you for your kind letter of December 29, notifying me that I am now a Life Member of the Medical Society of the District of Columbia, and, therefore, exempt from further dues and assessments.

The Society has been a source of inspiration and interest to me always, and it is my hope that the good work of the Society may continue with increasing usefulness.

With kind regards and best wishes for the New Year, I am,

Sincerely,
V. B. JACKSON"

"January 14, 1937.
My dear Dr. Conklin:

Your very gracious letter of December 29, 1936, notifying me that pursuant to Chapter II, Article IV, of the Constitution I had been placed in the list of Life Members, came as a surprise, as I had supposed I had another year to go as an Active Member. I was calculating from my entrance into the Society and not from my entrance into the old Association.

I take this opportunity to make a statement which I think would be well for the younger members to consider, viz., I do not think I ever attended a meeting of the Medical Society in all these 40 years that I have not come away with something to add to my store of knowledge. My interest in the Medical Society shall continue as always.

Very sincerely yours,
JOHN D. THOMAS"

Bills before Congress

Of Interest to the Local Profession

The Society, in session on the evening of January 6, 1937, formally accepted the report of the Legislative Committee, Dr. William Gerry Morgan, Chairman. The following bills, with minor changes noted, were approved:

H.R. 8158—A bill to amend an Act of Congress approved May 28, 1924, to regulate the practice of optometry in the District of Columbia.

The amendment to this bill merely stipulates that its provisions shall not apply to physicians and surgeons practicing under authority or license issued under the laws of the District of Columbia for the practice of medicine and surgery, and further, that it shall not apply to persons selling spectacles or eye-glasses who do not attempt to adapt them to the eye and who do not practice or profess the practice of optometry. Furthermore, the bill is not to prohibit the operation by any individual, firm, partnership or corporation in any mercantile establishment of an optometric department under the supervision, direction and management of a regularly licensed and registered optometrist. Your committee finds nothing objectionable to the provisions of the proposed bill.

S. 2153—A bill to provide for the prevention of blindness in infants born in the District of Columbia.

Section I. (a) That the words "*prepare and place*," where they occur in the language of the bill, be stricken out and instead of this language the word "*provide*" be inserted. This recommendation is made because the Health Office of the District of Columbia does not in fact prepare and put up silver nitrate or other silver preparations, nor is it deemed practicable that the Health Department should undertake to do this. The suggested change in the bill would favor the purchase of suitable silver preparations for the purpose indicated.

(b) Following the words "*administer it*" insert "*immediately upon delivery*." Your committee believes that the recommended insertion will make clearer the use of silver nitrate as a prophylactic for the indicated purpose.

Section II. The committee recommends that the bill provide, if possible, authority for the Health Department to secure the forceful transferral of infants suffering from acute ophthalmia to hospitals where proper treatment can be given. The committee specifically recommends that the word "treatment," where this occurs in this Section, be amplified to include hospitalization, where deemed necessary, by the health authorities. The committee further recommends a change of the wording of this Section, substituting the word "*Department of Public Works*" for "*Health Department*." The practice in the District of Columbia at the present time places the expenditure for treatment of the indigent sick upon the Board of Public Welfare. Hospitalization of infants afflicted with ophthalmia should, therefore, follow this practice.

Action was withheld by the Society on the following, upon recommendation by Dr. Morgan:

S. 3513—A bill to amend an Act entitled "An Act to regulate the practice of pharmacy and the sale of poisons, and for other purposes."

S. 3084—A bill to regulate the practice of pharmacy in the District of Columbia.

Medical-Dental Service Bureau, Inc.

Representatives

The following were re-nominated pursuant to action of the Society, in session on the evening of January 13, 1937, to represent the Medical Society of the District of Columbia on the Board of Directors of the Medical-Dental Service Bureau, Inc., for the year 1937:

Thomas A. Groover
J. Russell Verbrycke, Jr.
Henry C. Macatee
Oscar B. Hunter
Harry S. Bernton
Wallace M. Yater
Coursen B. Conklin

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS

The regular meeting of the Washington Society of Pathologists was called to order at 1:30 P.M., December 3, 1936, in the Army Medical Museum by the President, Dr. Roger M. Choisser. The Council reported favorably on the nomination of Dr. C. H. Binford as an associate member and of Dr. Robert J. Jermstad as an active member and both were unanimously elected. Dr. J. W. Lindsay introduced Drs. C. H. Grazier and W. T. Langston. Major J. E. Ash, a former president of the Society and the new curator of the Army Medical Museum, was presented by Captain Elbert DeCoursey.

Scientific Paper

"Adrenal Death." **Captain Hugh R. Gilmore, Jr.**, Army Medical Museum.

Two cases were presented in which it is believed death was due to adrenal insufficiency. The first case was that of a woman 53 years of age who 6 years previous to her death had had a radical amputation of the left breast for carcinoma. She made a good recovery. Except for occasional attacks of indigestion in the past year she had been in good health until about 2 weeks before her death when she developed nausea and vomiting being unable to retain any nourishment. She complained of some indefinite abdominal pain but had no localizing signs. There was only a very slight elevation in temperature in the last few days of her illness. Forty-eight hours before her death she became comatose and did not arouse from this state.

At autopsy both adrenals showed metastatic carcinoma, which in the right adrenal appeared to replace all adrenal tissue. The left adrenal showed a small portion which grossly was not invaded by the tumor. There were also small metastatic carcinomatous lesions in the right lung, bronchial lymph nodes, liver, kidneys and in the right ovary. No X-ray films were taken to rule out metastases to bones. The metastatic lesions in the lung, liver, kidney and ovary were small and were not thought to be of sufficient extent to cause death, while the lesions in the adrenals had destroyed most of the adrenal tissue.

It is believed that death here was due to adrenal insufficiency more particularly cortical insufficiency. The sudden onset of symptoms with gastric symptoms predominating and the comparatively rapid course of the last illness fit in with the picture of cortical adrenal insufficiency as described by various authors.

The second case was that of a white male, aged 20, a Civilian Conservation Corps enroller. On July 15, 1936, he developed abdominal pain just after arising in the morning. He reported to the dispensary and was given pills. The next day he was no better and on the following day, July 17, he was admitted to the hospital complaining of nausea, vomiting, abdominal pain and general weakness. The blood pressure on admission was 124/70. Food was restrained for 24 hours and the patient improved. Pain and vomiting ceased but the patient still was weak and had no desire for food. On July 21 he suddenly went into a state of shock with cold, clammy skin and rapid pulse. The blood pressure dropped to 70/40. In spite of stimulants, etc., he died the next day. There is no mention in the physical examination of any skin pigmentation nor is there any history of previous ill health.

At autopsy the thymus was found enlarged, weighing 40 gm. The heart was small, weighing 270 gm. The adrenals were small but weights were not given. The specimen of adrenal received for histological examination was quite thin, much thinner than the average adrenal, measuring only 8 mm. through the thickest portion and 2 mm. through the thinnest portion. The usual cortical pigment was not recognized. No medullary tissue was seen grossly.

Microscopic examination showed some hyperplasia of the thymus and a moderate increase of lymphoid tissue in the wall of the stomach. Other portions of the intestinal tract were not received for examination. Sections of the adrenal showed atrophy of the cortex with infiltration of lymphocytes and increase of connective tissue. Only occasional islands of cortical cells were present and these were frequently larger than usual, showing acidophilic, granular cytoplasm. No medullary cells were seen. The histologic appearance did not suggest tuberculosis.

This was considered a case of cortical adrenal insufficiency or idiopathic Addison's disease. In his original description of the disease known by his name, Addison described both cases in which tuberculosis of the adrenal was found and other cases presenting the same symptoms in which no tuberculosis was found. The enlarged thymus, hyperplasia of lymphoid tissue of the intestinal tract and a small heart suggests status thymicolymphaticus which is mentioned by several authors as being associated with hypofunction of the adrenals.

It seems surprising that death should occur so suddenly when the disease process is obviously of some months' duration, yet such sudden death is not unusual in these cases. In his book "Pathology of Internal Diseases," Boyd mentioned the case of a soldier who had been doing active duty and died suddenly. At autopsy the right adrenal was destroyed by tuberculosis and on the left only a narrow strip of cortex was left.

In the discussion **Dr. J. W. Lindsay** presented 2 slides from 2 cases of adrenal insufficiency with tuberculosis. One of these cases had a systolic blood pressure of 200 or 250. Operation had been done for the relief of the hypertension and a very hard adrenal was found on the side it was done on first, and within the last 2 or 3 weeks the other side was examined and a biopsy from that shows no characteristic changes. **Dr. Harry A. Davis** stated that there have recently been reported cases of adrenal insufficiency following operation on the adrenal gland. About 6 months ago Dr. Rudolph of Chicago described a case in which adrenalectomy had been done for diabetes mellitus, based upon the work of Long of Philadelphia who showed that glycosuria might be diminished by throwing out the medulla. After operation there were typical symptoms of Addison's disease. Usually, complete replacement of the medulla with fibrous connective tissue and lymphoid hyperplasia of the liver followed acute denervation of the adrenal glands for hypertension, and Addison's disease developed. There may be a vascular necrosis of the adrenal gland. Removal of adrenal gland often results in thyroid hyperplasia. **Dr. G. B. Dowling** cited a case in which there was a Neisserian infection and arthritis. Typhoid vaccine was given intravenously, and after the second injection the patient died in shock. Autopsy revealed hemorrhage in both adrenals. **Major Welsey C. Cox** said that in Walter Reed General Hospital a large series of cases had been studied in which the adrenals played an important part in the pathologic picture. The first case was an acute death in a CCC enroller who was a middle-weight boxer and who did heavy work in a gravel pit. On Friday night he engaged in a boxing bout and on Saturday morning complained of slight weakness and some nausea. He was not ill enough to be treated at the dispensary but he quit working and went home. On Sunday he was very much worse. No diagnosis was made, but the man evidently was in very complete shock. He developed an eruption all over his body. Rocky Mountain spotted fever was suspected. Monday morning his blood pressure was very low and he died within a few minutes after coming to the hospital. Necropsy revealed nothing grossly. Tests were negative for spotted fever. The most striking thing was the hemorrhage in the adrenals, the medulla of which was practically destroyed. Careful examination showed gram-negative diplococci in the meninges, indicating a very early case of fulminating cerebrospinal meningitis with symptoms of collapse. The second case was that of a veterinary officer who had a normal blood pressure until the onset of illness in 1935 when he suddenly started having cerebral attacks and his blood pressure became very high. A very large tumor was found in the left adrenal, extending into the inferior vena cava, and metastasizing in the brain. The adrenal gland is being extracted and tests will be done on the medullary substance. He had a very unstable blood pressure, sometimes a systolic of 250 and again of 160. There were no blood sugar tests. **Dr. E. Clarence Rice** discussed a fulminating case of epidemic cerebrospinal meningitis which terminated within 24 hours. He also told of 2 cases of diabetes which in the past 2 years have had all the symptoms of adrenal insufficiency.

Presentation of Cases

Dr. Harry A. Davis presented slides from a colored female, aged 20 years, who for a year prior to admission to hospital had been complaining of abdominal pain and profuse vaginal discharge. Three months before admission the pain localized in the lower abdomen, and when she was admitted physical examination revealed a pelvic abscess. Some fever and night sweats had been present. A posterior colpotomy was performed and a pelvic abscess drained. A draining sinus developed in the right groin, and after a protracted course and increasing anemia the patient died. At autopsy a large pelvic abscess was found communicating with the right fallopian tube and extending into the rectum, urinary bladder and ileum. Microscopic examination showed actinomycotic ray fungi present.

The discussion centered about the question of our ignorance in regard to the route by which actinomycosis arrived in the oviducts or ovaries. Some doubt as to this case being actinomycosis was expressed.

Dr. C. H. Binford presented first a case of a 39-year old white man who was hospitalized, March 11, 1936, with complaint of colicky pains just above crest of the right crest of the ileum. There were hematuria and a 15- to 20-pound loss of weight. Cystoscopic examination with pyelogram revealed considerable right hydronephrosis and evidence of a vessel producing an obstruction of uretero-pelvic junction. The right kidney was removed. It and surrounding tissues were involved in a tumor mass. The surgeon's diagnosis was hypernephroma. Sections were submitted to the National Institute of Health and this case was presented at the April, 1936, meeting when the diagnostic opinions were divided between metastatic carcinoma and primary multicentric granular-cell carcinoma. The patient returned to hospital, July 2, 1936, with a mass in the epigastrium, abdominal cramps, and sacro-iliac pain. The roentgenologist described destruction and increased density of the body of the first lumbar vertebra which he thought typical of metastatic carcinoma from the prostate. Autopsy on October 2, 1936, showed a large tumor mass about at the site of right kidney extending to but grossly not invading the vertebrae, and metastases to the right adrenal and regional nodes; 80 per cent of the liver was replaced by metastatic tumor. The prostate and testes were negative. Histopathologic diagnosis: Multicentric granular-cell adenocarcinoma arising in sclerotic right kidney probably on the basis of an old hydronephrosis, with local postoperative recurrence and metastasis to regional lymph nodes; right adrenal and liver and tumor emboli in pulmonary arterioles; bronchopneumonia.

In the discussion the consensus was consonant with the diagnosis of primary kidney carcinoma.

Dr. Binford secondly presented the case of a white man, aged 49 years, with a clinical diagnosis of pulmonary tuberculosis, chronic, far advanced, and a history of tuberculosis since 1925. The sputum was repeatedly positive for tubercle bacilli. At autopsy the surfaces of both lungs were ragged and torn due to separation of adhesions. There was a large cavity about 3 cm. in diameter in the upper outer part of the lower left lobe. The right middle lobe contained many multilocular cavities. Both apices presented circumscribed areas of softening about 5 cm. in diameter containing black, putty-like material and surrounded by fibrous tissue. The left lung weighed 1,475 gm., the right lung, 1,100 gm. Histopathologic diagnosis: Anthracosilicosis of lungs and peribronchial glands; tuberculosis, pulmonary, chronic; tuberculosis of colon and liver; periaortitis, probably syphilitic; nephrosclerosis, slight, focal, arteriolar; chronic passive congestion of liver and spleen.

In the discussion it was stated that with the polarizing microscope silicosis granules are demonstrable. **Dr. J. W. Miller** stated that it is difficult to make a diagnosis of anthracosilicosis in patients treated in Pennsylvania who work in coal mines. In patients treated there no signs of tuberculosis were found; they all had typical anthracosilicosis; there was a vast amount of carbon pigment present. One would be perfectly safe in making a diagnosis from autopsy material of anthracosilicosis; chemical analysis, which is rather simple, should be run, and, also, acid-fast stains should be done. The diagnosis of tuberculosis with the combination of anthracosilicosis is exceedingly difficult, and the only sure indication is the demonstration of bacilli. Tuberculosis is a natural sequela of silicosis. Occupational histories are large factors in the diagnosis.

Dr. Binford presented also a case of a white man, aged 43, who was admitted to hospital complaining of nausea, vomiting, weakness and an occasional aching pain in the abdomen. His condition became progressively worse and he died 13 days after entering the hospital. R.B.C., 4,770,000; Hb., 84 per cent; W.B.C., 17,100. Wassermann negative. Weight 185 pounds in 1929. Diagnosis: Cholelithiasis with jaundice and chronic and acute inflammation of common duct and pancreatic duct; hyperplasia of smaller pancreatic ducts and intrahepatic bile ducts; obstructive cirrhosis of liver; and adenocarcinoma of duct type in pancreas involving the lymph nodes and pyloric wall; acute and subacute local peritonitis; arteriosclerosis, local. The pancreas grossly showed several cystic areas with papillomatous infoldings of hypertrophied epithelium. No gallstones were found.

The discussion concerned points in clinical diagnosis.

Dr. L. L. Ashburn presented a case of a white male, aged 38 years, who for the past year and a half had pain in his legs, weakness, lassitude, loss of appetite and loss of weight. He fell down 4 steps and fractured the right and left femurs, the right humerus and the right clavicle. Laboratory data: R.B.C., 3,310,000; Hb., 75 per cent; W.B.C., 7,600; Kahn test negative; PSP, 20 per cent in 2 hours; Mosenthal, reduced function; blood calcium, 14.7 and 16.9 gm.; blood phosphorus, 3.4 and 2.7 gm.; blood sugar 80 mgm. At operation an enlarged left parathyroid gland was removed measuring 2.5 by 3.5 by 4.5 cm. Microscopically, a glandular tumor was present.

In the discussion a majority of opinions favored the diagnosis of malignant tumor, rather than of an adenoma.

Dr. Vincent J. Dardinski presented a specimen taken from a cadaver showing the testicle on the right side attached to the spermatic cord. A tumor was found along the spermatic cord in the canal. This cadaver looked to be about 42 to 50 years of age. Its structure is that of an adenoma of the cells of Leydig (interstitial cells of the testis).

In the discussion opinions were varied both as to the origin and as to the degree of malignancy, adenocarcinoma of unknown origin and benign adenoma being mentioned. In some parts the tumor seems to be invading the capsule but the inner cells do not look malignant. Since the cells are characteristically nuclear, they fit Ewing's description of adenoma of interstitial cells of the testis.

Dr. Oscar B. Hunter presented frozen sections from the case of a white man, aged 60 years, who had a pedunculated mass on the lateral aspect of the tongue, somewhat "mushroom" in shape. The superficial surface was ulcerated. There were enlarged glands in the cervical region. The tissue submitted for examination consisted of a somewhat pyriform mass measuring 2.5 cm. in its longitudinal diameter by 1.2 cm. transversely and 1.1 cm. in thickness; it was fairly soft in consistency, cut without increased resistance, and presented a more or less "meaty" appearance; it appeared to be covered, in part, by epithelium, whereas other portions showed a raw surface.

Discussion brought out the possible diagnoses of rhabdomyosarcoma and of fascial fibrosarcoma. All agreed the tumor was malignant.

Dr. Hunter also presented the case of a white woman, aged 57 years, whose menopause occurred 5 years before. Last spring she became fatigued, and in June she had a small vaginal hemorrhage. Other hemorrhages occurred in August and again in September. Since the last hemorrhage the patient had a bloody discharge which cleared up after several days in bed. She had lost 5 pounds, and since September, 1936, had noted an increasing weakness. Upon admission to the hospital the bloody discharge became less profuse; a diagnostic curettage was performed and radium inserted in the uterus. After a diagnosis of smooth-muscle sarcoma, radium was inserted and the uterus packed.

In the discussion it was decided that further staining and study were necessary before a conclusion could be drawn.

Dr. Robert J. Jermstad presented the entire anatomic specimen of a case of congenital bilateral hydronephrosis. The fetus was so large that decapitation was performed during labor, without helpful effect. The tremendous size of one pelvis without demonstrable adjacent kidney parenchyma made obscure the origin of the fluid content. Urethral and ureteral valves were demonstrated as the cause of the hydronephrosis.

Dr. R. D. Lillie presented the case of a white man, aged 65 years, an engraver. Carcinoma of the stomach was diagnosed, February, 1934, by X-ray and clinically. He returned to hospital in September in coma with a history of gradually increasing drowsiness, loss of weight, and cachexia, and died 6 days later. At autopsy a polypoid tumor in the stomach 5 cm. from the esophagus was found. There were some serosal and omental nodules, and white firm areas in the cortex of the right kidney. The lungs were negative; the right apex was scarred. There was advanced aortic atheroma. Microscopically an acute miliary tuberculosis of the lungs, liver and spleen was found. There were caseous infarcts in the right kidney, old and recent tuberculosis in the bronchial lymph nodes. Diagnosis: papillary adenocarcinoma of stomach, metastatic to regional nodes; general arteriosclerosis.

Dr. Lillie also presented the case of a white man, aged 42 years, restaurateur. He had been ill 3 months with gastric symptoms, ascites, and persistent vomiting. X-ray was unsatisfactory. The lower end of the esophagus was obstructed, with little barium in the stomach. He died 4 weeks later. Autopsy showed ascites, moderate atherosclerosis and a hard tumor encircling the stomach toward the cardia and invading the omentum, colon and spleen. There were multiple metastases in the liver. Microscopically, there was a diffuse carcinoma simplex of the stomach with omental lymph node and splenic extension, liver metastasis and fibrocaseous and cellular tubercles in the upper lobe of the right lung.

Dr. Lillie also presented the case of a white seaman, aged 60 years, whose onset of illness was in March, 1935. After a diagnosis of carcinoma of the rectum a colostomy was performed, October, 1936. There was a gradual decline during the following year. He died, October 15, 1936. Grossly, there were carcinoma of the rectum, metastasis to the liver, and metastatic nodules in the lungs (?). Microscopically adenocarcinoma of the rectum, metastases in the liver, miliary and conglomerate fibrosing and caseating tuberculosis of the lungs with acid-fast bacilli, areas of monocytic and fibrinous exudate and obliterative arteriosclerosis were found.

Dr. R. M. Choisser presented a case of a white woman, aged 52 years. She was well until 2 years before, when she developed a feeling of pressure in the pelvis with polyuria. Physical examination revealed what was thought to be a fibromyoma of the uterus. Operation, November 15, 1936, revealed bilateral fibroids of the ovaries, which were removed. The uterus was small and of the senile type. Sections showed complete replacement of both ovaries by fibrous tumors, together weighing 520 gm.

Meeting adjourned at 4:15 P.M.

COMING MEETINGS

Wednesday, February 3: Business Meeting. Reports of committees.

Wednesday, February 10:

1. "Evil effects of Dinothrothenal with Particular Emphasis on Cataracts." William Thornwall Davis, M.D.
2. "Recent Changes in the Therapy of Peptic Ulcer." Edward L. Howes, M.D.

Wednesday, February 17:

1. "Results Obtained in Functional Problems with X-ray and Glandular Therapy." Jacob Kotz, M.D., and Elizabeth Parker, M.D.
2. "Some Physical Bases of Mental Disorders." F. A. Moss, M.D.

Wednesday, February 24: Program will be furnished by the *Washington Society of Pathologists.*

1. "The Pathology of the Lungs and Other Organs in Silicosis." Philip B. Matz, M.D.
2. "Seasonal Variation in the Brain Reaction of the Saint Louis Encephalitis in Mice and in Endemic Typhus in Guinea-pigs." R. D. Lillie, M.D.

THE DAVIDSON LECTURE

On October 13, 1937, will be given the Fourth Davidson Lecture. Candidates for consideration must observe the following:

> "The selection of the Davidson Lecturer shall be on the basis of competition, the winning essay to be selected by a subcomittee consisting of five (5) members of the Executive Committee appointed by the Chairman. No member can serve on the committee who may desire to compete.
>
> The competition shall be thrown open to physicians or other scientists working in the District of Columbia.
>
> The essays to be submitted must bear no indication of the author's identity, being signed by a nom de plume. The identification of the author must be in a sealed envelope bearing on its surface the same nom de plume. No essay may be submitted that has been published.
>
> Essays should be submitted to the Secretary of the Medical Society of the District of Columbia not later than the first of July of odd number years.
>
> In case no essay is found worthy of an award, the subcommittee shall declare no award; the lecturer then to be selected by the full Executive Committee."

Dr. Francis X. McGovern is the Chairman of the Subcommittee of the Executive Committee. It is desired that as much publicity be given the opportunity afforded Washington physicians as possible. Fellows in the two local Schools of Medicine or anyone else having work, the result of their own research activity, are especially urged to submit prospectus. Communicate with Dr. Francis X. McGovern's committee now. The selection will be made after closing date, July 1, 1937.

ANNUAL SCIENTIFIC ASSEMBLY

MAY 5–6

Dr. Howard W. Haggard announced as speaker at Public Meeting, Wednesday evening, May 5

Plans are proceeding for an outstanding program which in all probability will bring the largest attendance enjoyed at these meetings. Sessions will be held all day Wednesday and Thursday. The Public Meeting, to which members are urged to invite their clientele, will have as guest speaker, Dr. Howard W. Haggard, Associate Professor of Applied Physiology, Yale University. He is the author of "Mystery, Magic and Medicine," "Devils, Drugs and Doctors," "The Science of Health and Disease," and other popular books, as well as scientific treatises. Dr. Haggard has a national reputation as a speaker on medical topics to lay audiences.

The Thursday night banquet will have suitable features for entertainment of the physician and his family.

Note these dates now.

NEWS AND PERSONALS

The Pan American Medical Association, Washington, D. C., Chapter, held their meeting at the home of Dr. James Alexander Lyon, in Rockville, Maryland, January 10, 1937. The President, Dr. Henri de Bayle, Minister of Nicaragua, presided, assisted by the Secretary, Dr. A. A. Moll. The program:

1. "Recollections of Medical Practice in the Tropics." Dr. Augusto S. Boyd, Minister of Panama.

   A comparative picture of surgical and medical conditions in the Tropics and Temperate Zone was made, with a detailed analysis of diseases most prevalent in Panama, value of spinal anesthesia, factors that should guide treatment, indications and rules that should govern the use of surgery, management and postoperative care in cases complicated with malaria and intestinal parasites, by a surgeon with more than 30 years' practice and head of one of the largest hospitals in Latin America.

2. "Gallbladder Disease: Diagnosis, Management, and Prevention." Dr. B. B. Vincent Lyon, of Philadelphia.

   A thorough and authoritative presentation was given, with a series of unique lantern slides, showing the various phases of the subject, stressing the prevalence of cholecystitis and cholelithiasis, errors in diagnosis, and especially prevention; and selection of proper cases for medical and surgical attention.

Dr. Isidro Castillo, Professor of Surgery, Buenos Aires Medical School, expressed his thanks for the cordial welcome met by Latin American physicians in the United States, especially at the hands of the Pan American Medical Association. Other out-of-town guests included Dr. Hugh H. Young, Baltimore; Dr. W. Wayne Babcock, Philadelphia; and a group of Latin American physicians taking postgraduate courses at Johns Hopkins University. About 90 Washington physicians attended the meeting.

The Smith-Reed-Russell Lecture was held in the George Washington University School of Medicine, January 21, 1937. Rear Admiral Charles S. Butler, Medical Corps, United States Navy, was the guest speaker; his subject, "The Public Health Importance of Syphilis."

The University of Louisville School of Medicine, the second oldest School of Medicine now in existence west of the Alleghanys and the oldest municipal medical college in the United States, celebrates its centennial, March 31–April 3, 1937, at Louisville, Kentucky. The alumni are urged to make their plans now to attend.

Dr. Joseph S. Wall, Professor of Pediatrics, Georgetown University School of Medicine, by invitation addressed the George Washington Alumni Medical Society, December 19, 1936, on the subject, "Preventive Immunization in Childhood."

Dr. Custis Lee Hall received on January 4, 1937, the citizenship cup award for meritorious service rendered to the people of Washington during 1936. Commissioner Melvin C. Hazen made the cup presentation. Under the auspices of a local newspaper a committee made up of representatives from the Federation of Citizens' Associations, Federation of Business Men's Associations, District of Columbia Bar Association, Board of Trade, District of Columbia Congress of Parent-Teacher Associations, Merchants and Manufacturers Association, District of Columbia Federation of Government Employees, Federation of Women's Clubs, and the Medical Society of the District of Columbia, annually make the award with the following objectives:

(1) As a reward to the resident of Washington who, during the year, has rendered outstanding, unselfish service to the people of Washington; (2) in order to call such exemplary service to the attention of the public; (3) that by this good example, all the people of Washington may be stimulated to perform such noble service to the extent of their capacity and opportunity for benefit of all the public of Washington.

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RECENT ADVANCES IN PROCTOLOGY*

GARNET W. AULT, M.D.
Professor of Proctology, Georgetown University School of Medicine

During the past several years there has been an increasing and noteworthy effort to place before the medical profession many new and excellent procedures in the treatment of anorectal disorders. Physicians who are not intimately familiar with anorectal disease are often given a false sense of security by the glowing reports of the enthusiast who admits of no failure. In contrast, a method may receive the unqualified condemnation of an individual who has been unable to duplicate the feats of its originator. As a result, we are all confronted with the problem of selecting the method of choice to be used in our individual cases or series of cases. Therefore, in presenting this subject to you due regard is given to the therapy that produces the most constant satisfactory results in the hands of the greatest number of individuals. In addition, some attempt will be made to individualize the management of certain disorders.

Before we consider the individual subject matter it would seem pertinent to remind you that the man in general practice is the individual who is often first consulted for "piles" and that the ultimate fate of the patient is, to a great extent, in his hands. He may have "piles" or he may have cancer. The diagnosis can be made only by examination, not by history. If the medical profession, the medical student and the laity could be impressed, to a greater degree than heretofore, that bleeding by rectum is due to a malignant lesion until proven otherwise, much would be accomplished. When proper examination has been made and the diagnosis has been established, the physician who makes judicious use of the recent additions to the armamentarium of proctology will be rewarded with an increasing incidence of excellent and permanent results. Thus, the misdirected use of the various methods will be avoided and the procedures will not fall into disrepute with either the laity or the profession.

HEMORRHOIDS

This condition attains first rank among anorectal diseases, since it may be stated safely that approximately 12 per cent of individuals have hemorrhoids.

The phase of the treatment of hemorrhoids that has been brought to our attention for many years is the controversy being waged relative to the injection versus the operative treatment. No attempt will be made here to settle that dispute. However, attention will be drawn to the fact that we are inclined to be enthusiastic about something that is an economic blessing to our patient. I refer to the ambulatory injection treatment of hemorrhoids. We are inclined to swing too far to extremes, and today the injudicious use of the injection treatment of hemorrhoids is productive of considerable dissatisfaction, and even harm, to a great many patients. The number who receive injection treatments for hemorrhoids, in the presence of undiagnosed cancer, has been given as 10 to 30 per cent by various authorities. Surgical hemorroidectomy is also guilty of the same error in approximately the same percentage of cases. Therefore, it behooves us to take inventory of ourselves if we have, in any way, contributed to this group of unfortunate cases.

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*Read before the Society, December 16, 1936.

INJECTION TREATMENT OF HEMORRHOIDS

The injection treatment of hemorrhoids aims, by the process of chemical inflammation, to be productive of 3 effects upon the tissues injected: (1) To induce an inflammatory sclerosis of the tissues; (2) to thereby obliterate the vascular spaces of the hemorrhoidal mass; and (3) to produce such a physiological ligation of the tissues that shrinkage, fixation and atrophy of redundant tissues occurs.

The histopathological changes occurring in the injected tissues have been known for many years. It has taken considerably longer to evaluate the results of therapy and, in retrospect, to state the type of case suitable or unsuitable for injection. We are prepared to make very definite statements regarding these groups as the ultimate outcome of these patients is known from many years of follow-up study.

1. *Group Suitable for Injection.* It is universally accepted and taught that the uncomplicated internal hemorrhoid is the only hemorrhoid which is not only suitable for injection, but that it is also the only one that responds with any degree of permanent result to the injection. This soft vascular pile should protrude little if at all. Protrusion or extension of the mass external to the sphincter renders it less amenable to the injection treatment. The soft, pliable, vascular mass which is about the diameter of an ordinary lead pencil, or less, responds favorably to the injection treatment. Marked inflammation, erosion or ulceration, if present, should be decreased by temporary palliative measures such as sitz baths or retention enemas of warm oil. In the presence of complicating fissure, ulcer, fistula, polyp, etc., the hemorrhoids are best treated by operative procedures aimed to correct the complicating condition and the hemorrhoids at the same time.

2. *Group Unsuitable for Injection.* There are many cases of internal hemorrhoids of long duration that have attained considerable size. This is probably the case that presents itself to you with an anus and lower rectum encircled by a mass of hemorrhoidal tissue. In contrast it may be the case that has 1 or 2 large thumb-sized internal hemorrhoids and the rest of the anal canal is not involved. In the early stages these hemorrhoids prolapse and return spontaneously to within the rectum. Later the prolapse requires manual reduction of the pile mass and by this time the sphincter has become markedly atonic. These cases are unsuitable for injection therapy because the temporary cessation of hemorrhage and the shrinkage of the mass is transient and recurrence within 6 months to 2 years is common. Many of these cases may develop a hard fibrotic tumor mass that will readily prolapse through the sphincter and produce considerable discomfort and pain which may be more severe and disconcerting than the original lesion. Prolapse, thrombosis and edema have been known to develop after injecting this type of hemorrhoid, and the resultant painful, ulcerating, sloughing mass is truly "an attack of piles." These cases of massive internal hemorrhoids should be recognized as unsuitable for injection treatments except as a palliative measure in exceptional instances.

Fibrous internal hemorrhoids or polypi of any type are unsuitable for injection.

External cutaneous and external varicose hemorrhoids should never be injected under any circumstances at any time. Painful, disastrous and disabling results will follow upon the injection treatment of external hemorrhoids.

The last group, the combined internal and external hemorrhoid, in general is unsuitable for injection therapy. In these cases of combined hemorroids both the patient and the physician should be aware of the limitations of the injection treatments. There are many who make a practice of injecting the internal portion of this type of hemorrhoid. The amount of sclerosis, shrinkage and obliteration that takes place in the internal portion of the hemorrhoid is frequently sufficient to produce a diminution in size of the external mass, due to a loss of venous anastomosis between the two areas. Symptomatic relief of hemorrhage is attained and if this has been the most troublesome symptom, the patient and the physician are satisfied. The cautious use of injection therapy to this type of hemorrhoid is urged from a conservative standpoint. Both the patient and the physician are inclined to expect too much from a needle and a syringe filled with solution. I think that it is a matter of record that the injection treatment of this type of hemorrhoid is responsible for the unsatisfactory results reported from time to time. This is indicated by the variations noted in reporting the incidence of hemorrhoids suitable for injection.

We have statistics indicating that from 80 to 90 per cent of hemorrhoids are suitable for injection. I feel that this is a clear case of enthusiasm that will be dampened by proper follow-up of these cases, as recurrence is usual. The reported high percentage of injections is not in keeping with the observations of such authorities as Yeomans, who states: "Only about 50 per cent of cases of internal hemorrhoids are suitable for injection," and Gabriel, who "estimates that the allocation of treatment at the present time (1932) is about 50 per cent injection and 50 per cent operative." It is pointed out that earlier (1929–1931) Gabriel, in his enthusiasm for the injection treatment of hemorrhoids, had previously reported on 800 new cases of hemorrhoids in which the injection treatment had been used in approximately 75 per cent. Referring to combined internal and external hemorrhoids Gabriel further states: "That as a result of increasing experience I have become extremely cautious about injecting this type of case." The above authors, and others in authority, have indicated that the incidence of cases of internal hemorrhoids that are suitable for the injection treatment is closer to 50 per cent than to the higher figures. My own personal experience leads me to believe that for desirable permanent results, the injection treatment of internal hemorrhoids should be restricted to less than 50 per cent of cases. If temporary alleviation of symptoms is to be the goal of the treatment, then a greater number than 50 per cent of cases may be injected, but in fairness to both physician and patient, the limitations of this mode of therapy should be known.

Technic of Injection. A complete proctosigmoidoscopic examination is indicated before any treatment is administered. All agencies and physicians interested in cancer have repeatedly urged that we eliminate malignancy of the rectum and pelvic colon as the first cause of rectal bleeding.

The anoscope is inserted full length, the obturator removed and under direct vision, aided by good illumination, the anoscope is gradually withdrawn. The hemorrhoids will protrude into the lumen of the instrument as it is withdrawn, and all hemorroidal masses above the anorectal line are identified. The mucosa of the upper pole of the hemorrhoid is swabbed clean. Antiseptic applications are not necessary. The needle is inserted into the submucosal tissue and a painless infiltrating injection of solution is made. According to the choice of the operator 5 per cent phenol in vegetable oil or 5 per cent quinine and urea hydrochloride in sterile distilled water are used. An average of 2 or 3 cc. of solution is injected. Injections are given at 3 to 5 day intervals, and several weeks are allowed to elapse before a given quadrant or mass is reinjected.

The details of the injection should be scrupulously followed. The injection should be made slowly into the tissues and just enough solution used to produce moderate distention of the mass. Blanching of the mucosa indicates that the injection is too superficial or that too much solution has been used. Slough will follow either technical error. A properly placed injection, above the anorectal line, is painless, and the patient should note only a slight sense of fullness or pressure in the rectum. The injection should be placed at the upper pole of the hemorrhoid.

Results. The immediate results of the injection treatment of hemorrhoids are most satisfactory to the patient and to the physician. Pain, prolapse and bleeding are immediately controlled in properly selected cases. As a palliative measure in pregnancy, advanced cardiorenal disease and in other conditions, the injection treatment has considerable merit. The permanency of results will vary and one should give considerable thought to this phase of the method. In general, the injection treatment of hemorrhoids is considered to be safer from many standpoints than the operative treatment. Recurrence is definitely more frequent after injection than after operation.

In conclusion, we may consider that the uncomplicated internal hemorrhoid of small or moderate size may be permanently cured by the injection method. The larger internal hemorrhoid will recur. Injection of the internal portion of the mixed internal and external hemorrhoid is of no value except as a temporary measure in a few properly selected cases. These results may be obtained only if the physician properly evaluates the limitations of the injection treatment of hemorrhoids.

Fistula

The treatment of fistula is rarely, if ever, an ambulatory management. This constitutes a hospital procedure which is best carried out under the influence of an anesthetic which relaxes all of the muscles of the pelvic outlet, including the sphincters and the levator ani. We are all familiar with the patient who has had several "preliminary" operations. If we search for the cause of these "preliminary" operations we will be led to the conclusions drawn by Hirschman, Dudley Smith, Buie and others. In many cases it is due mainly to a confusion in nomenclature and an error in the conception of fistula in ano, and it, therefore, seems wise to briefly discuss the main etiological factors in this condition.

An understanding of the point of origin of fistula will be attained if one will briefly recall that the junction of anus and rectum is marked by a definite anatomical structure, the anorectal line. The anal crypts of Morgagni are in this area. They average 6 to 12 in number and they are the point of origin of over 90 per cent of all fistulae. Tracing the course of the infection, it will be seen that from this crypt or pocket, the infection spreads downward and outward. The course of the infection will vary in relation to the sphincters and to the minute anal glands which have recently been demonstrated by Tucker and Hellwig. The course of the infection may be superficial to the sphincter or it may involve it. Eventually the burrowing process appears on the skin surface as a perianal abscess. It may point in the ischiorectal fossa where it is commonly designated as an ischiorectal abscess. Rupture or surgical incision complete the process and a blind sinus or abscess pocket is converted into a fistula with both an internal and an external opening. Multiple tracts and sinuses may eventually develop but the point of origin of all may be traced back to an internal opening in a crypt of Morgagni.

MANAGEMENT OF FISTULA

A wider dissemination of the knowledge of the 3 cardinal principles in the management of fistula is indicated. These are as follows: (1) The identification of the internal opening; (2) the conversion of all fistulous tracts into open ditches which will be allowed to heal in and approximate from the base outward; and (3) the removal of all packing within 48 hours after operation.

The identification of the internal opening of all fistulae is best done at the time of operation. The injection of pastes or dyes through the external opening is a useful adjunct and is of considerable help in many cases. The paste or dye is identified as it escapes from the internal opening. The numerous ramifications and minute branchings of the fistulous tract are very easily identified if they are stained. However, it should be kept in mind that all tracts may not become stained and diligent search should be made for any unstained pathologic tissue.

Regarding the probing of these tracts, there are those who probe from inside out and those who probe from outside in. Let me urge you to learn to probe from inside out. Identify the internal opening, either with or without the aid of a dye. The probe should be a blunt-pointed, annealed silver instrument, and if it is gently inserted into the internal opening and worked through the main channel of the fistula the rest should be easy. No false tracts or openings into the anorectum are thus created, as does occur with those who probe from outside in. Probing into blind pockets, sinuses and the ramifications of the fistula from the outside constitutes a great insult to relatively normal tissues. More often than not a false opening into the anorectum is created and frequently the true internal opening of the fistula is lost. I feel sure that those who probe the fistula from the internal opening have fewer recurrences than those who probe from the outside in.

The idea of converting all fistulous tracts into open ditches which will be allowed to heal in and approximate from the base outward is based upon the principle of the healing of wounds about the anus. In general, suturing in an attempt to obtain healing by primary intention is unwarranted. Wounds and incisions about this area heal best by second intention and granulation. The soiled, infected field will heal satisfactorily if it is left open, but closure of the majority of wounds in this area is followed by stitch abscess, retention of pus, delayed and deformed healing. If we suture a fistulous wound the surface of the wound is prone to "bridge over" the tract, and with delayed healing of the deeper portion of the wound there is often a recurrence of the fistula. If we make a trench-like or saucer-like wound when removing the fistulous tract we should allow the wound to heal from the base upward. This approximation of healthy granulation tissue from the base upward assures us that no new tract is formed, and that the resultant firm scar, if severance of the sphincter was necessary, will act as a new bed of anchorage for the muscle.

The removal of all packing within 48 hours after operation is essential. Prolonged packing of the fistulous wound prevents wound approximation as outlined in the previous paragraph. When the sphincter has not been involved an anal canal which is prone to allow the escape of oil or liquid stool may follow. This is not a true incontinence but rather the result of a deep sulcus that cannot be completely effaced by muscular action. When the sphincter has been involved, the wide separation of its fibers from the resultant wound will be productive of a total muscular incontinence. Both of these conditions can be avoided by removal of the packing or dressing within 48 hours after operation.

In view of the foregoing it is felt that the management of anorectal fistula should be along the following lines. When a physician is called to open an anal abscess he should do so immediately, and, further, he should consider it to be the external opening of a fistula until it is proven otherwise. Following drainage and collapse of the cavity an effort should be made to determine whether an internal opening is present. Another type of case that may be encountered is the patient who presents himself to you after the abscess has ruptured. He may give a history of recurrent accumulation of pus accompanied by pain which is followed by a discharge of pus and a cessation of the pain. This may be a recent event or it may have been going on for some time. It is mandatory upon the physician to seek out the cause of the abscess in either case, and, if he will consider the lesion to be a fistula, the correct diagnosis will be arrived at in a rather high percentage of cases.

Fissure

Evidence points to the occurrence of this lesion in approximately 8 per cent of all anorectal disorders. This painful affliction of adult life may be indeed incapacitating, and the pain experienced at defecation may prostrate the patient. It is practical to divide fissures into 2 classes both from the standpoint of the morbid anatomy encountered and the treatment advocated.

ACUTE FISSURE

These relatively recent fissures may be a simple break in the anal skin or they may commonly appear as a friable postanal commissure, that cracks and bleeds at stool. Very little induration of the immediate area occurs and no granulation of the surface is noted. Frequently one will encounter small varicose buds whose skin covering is thin and friable. This type of fissure is really a recurrent skin cracking which is often brought on by the passage of a harsh abrasive stool or an irritant watery diarrhea. Within recent years the injection treatment of fissure has been advocated, and the methods used by Gabriel, Gorsch, Morgan and others are herein presented.

Technic of Injection of a Postanal Fissure. The patient is placed in the desired position and after preliminary skin sterilization a novocain wheal is raised in the skin about 1 to 2 inches posterior or distal to the anal margin. Five to 10 cc. of one of the new oil-soluble anesthetic solutions is injected into the deeper area. With the finger as a guide in the anal canal the postanal area is infiltrated with the oil-soluble anesthetic. A total of 5 to 10 cc. may be used. An even distribution of the solution is most desirable and pooling of the solution is to be avoided. The anesthesia and fixation will last from several days to 2 to 3 weeks, during which time the tissues will have improved their vascular supply and the fissure will have healed. This method of treating the acute fissure is a noteworthy contribution to the progress of proctology.

CHRONIC FISSURE

The chronic fissure is not only characterized by recurrence but also by its persistence. It is a chronic, ulcerated, indurated lesion with or without a sentinel pile at its lower pole. This infected tab of granulation tissue not only indicates chronicity and inadequate drainage of the area but it also indicates the type of treatment to be instituted for the adequate and permanent cure of the lesion. Surgical excision, rather than incision, is the treatment of choice.

Treatment of Chronic Fissure. Spinal, caudal or sacral block anesthesia are the anesthetics of choice, although infiltration anesthesia may frequently be employed in dealing with the smaller lesion. The entire mass should be removed by whatever method gives the best results in the hands of the individual physician, but the large excisions which remove the infected varicose tissue down clean to the muscle, represent the better method of caring for these lesions. The large triangular or racquet-shaped excision of the area will remove all of the pathologic tissues, and the internal or apex portion of the wound will heal before the external portion. Drainage is thus facilitated and bridging of skin or pocketing of tissues at the anus is avoided. Secondary fissure, ulcer, abscess, sinus and even fistula are avoided. These complications are known to follow when adequate drainage of the wound is not provided by the excision. This adequate removal of all the pathological tissue will result in a smooth anal margin.

PRURITIS ANI

The present status of pruritis ani is reflected in the voluminous literature available on this condition. Nearly all articles contain an elaborate classification of the causes, such as, systemic, general, remote, reflex, allergic, toxic, and so forth. The list is always the same and it is published and republished year after year with the order and arrangement changed a little.

At this time I wish to state that, in the light of our present knowledge, it is my firm opinion that all cases of true pruritis ani are due to a local pathologic condition in or around the anorectum. Furthermore, these patients will be found to comprise 4 rather distinct clinical groups that will be encountered in actual practice, as follows: (1) Cases with morbid anatomy that is productive of abnormal anal moisture, discharge or uncleanliness; (2) parasitic infestations of the anorectum; (3) dermatological lesions (fungi, etc.); and (4) chronic pruritis ani of obscure origin (infectious).

MANAGEMENT OF PRURITIS ANI

All patients should be studied and observed with sufficient diligence so as to eliminate them from the first 3 groups before they are placed in group 4. Time will not permit a detailed discussion of the procedures advocated, but a few points of interest will be mentioned. All infected hemorrhoidal tissue, infected sinuses, ulcers and fissures, and infected crypts are productive of a moist anal discharge. These lesions should be carefully evaluated and treated. The aid of a dermatologist may be necessary to determine the significance of a fungoid dermatosis. There are times when a vaginal discharge or a gynecological condition is responsible for a severe perineal and perianal irritation and the services of a gynecologist are indicated.

In dealing with patients with a pruritis of obscure origin, it seems obvious to even the most casual observer that the patient has already tried all the fancy salves, pastes, lotions, etc. To this effect we must eliminate, as a secondary factor, a dermatitis medicamentosa which has been added to our original process. The elimination of the drugs is indicated whenever possible. The recent investigations of Hirschman, Tucker and Helwig, and others have emphasized the rôle of the anal crypts and ducts in infection of the perirectal tissues in particular and in focal infections in general. I would like to emphasize that many of these intractable cases of pruritis ani should be investigated regarding a local diffuse low-grade tissue infection which has originated in the anal crypts and glands. No single organism is the causative agent in the light of our present knowledge. Further details on theory and experimental work are omitted for the sake of brevity.

Our present method of treating these cases belongs to the field of injection therapy, and with our present impressive array of solutions advocated for pruritis ani we should select with extreme discretion and caution the one best suited to our needs. We are confronted with the question of choice of procedure and choice of solution to be used. In this respect I feel that the injection of some of our newer oil soluble anesthetics is of considerable value. In contrast to the alcohols and acids they exhibit a less frequent tendency to slough, and although their effects are often not as permanent nor as efficient they are probably the safest solutions now available to the general practitioner.

Technic of Injection and Results. The general technic of using the oil-soluble anesthetics in treating pruritis ani will be given. It will, of necessity, require modification to meet the requirements of the various solutions available.

After preliminary skin antisepsis a novocain wheal is raised either about 1 to 1½ inches distal to the anal margin or just external to the line of demarcation of the pruritis. By dividing the area into segments 1 to 6 sites of injection are used. The first site is probably best located in the posterior commissure. No oily solution is to be injected intradermally if we are to avoid skin slough. A fan-shaped smooth infiltration of the solution is done into the deep subcutaneous and cellular tissues so that approximately 1 to 3 cc. of solution is injected in a given area. "Pooling" of the solution is to be avoided as this is liable to produce localized suppuration. The injection is relatively painless depending upon the individual reaction. New areas are injected at subsequent visits to the office and old areas are not to be injected again within a month to 6 weeks. The duration of the anesthesia and the extent of the obliteration of the tissue spaces with the oil-soluble anesthetics will vary with every case. Anesthesia may last longer than 3 weeks, and the relief of the pruritis will vary. Many cases are permanently relieved of their itching but it seems wise to point out that we should not expect more than 80 per cent of our cases to be cured by this procedure. Recurrence should be treated accordingly. Complications are uncommon with the oil-soluble anesthetics but they do occur in the form of abscess, sloughing and painful induration. The first 2 should be afforded free and adequate drainage and the latter should be treated along palliative lines.

ELIMINATION OF POSTOPERATIVE PAIN

The elimination of pain following rectal operations has been the quest of numerous investigators and we now have some occasion to feel hopeful that patients will be spared some of their undue suffering. Anorectal operations have enjoyed undesirable notoriety for years and it is common knowledge that patients will defer operation, or even consultation, rather than be subjected to the painful sequences of anorectal surgery.

If one is accustomed to do the ligature operation for hemorrhoids in which the base of the hemorrhoid is tied off and the remaining hemorrhoidal mass is excised leaving an open wound to heal by second intention, the following has considerable merit.

At the conclusion of the operation a small piece of gauze is soaked in a solution of eucupine base. This is a relatively nontoxic topical anesthetic of prolonged action which has, in addition, considerable bacteriostatic action. This topical application must be done before the general or spinal anesthetic has worn off. The gauze or cotton is pressed into the wound and the solution is applied every 3 hours for 4 times following operation. Prolonged use may delay healing. The surface anesthesia thus produced is welcomed by the patient, and although its action will vary slightly it is an excellent addition to this field.

The deep infiltration of one of the oil-soluble anesthetics has considerable value following hemorrhoidectomy and operations for fissure and fistula. A perianal infiltration is used and 5 to 10 cc. of the solution is spread around the anus and under the open wound areas. It should be carefully used in the presence of suppuration, as in fistula. The solution may be injected either at the beginning or at the end of operation according to the choice of the operator. The general rules and technic as already mentioned under pruritis ani are applicable.

With the topical application of eucupine to open wounds and the infiltration of one of the oil-soluble anesthetics adjacent to the field of operation we have at our disposal 2 excellent procedures aimed at the elimination of postoperative pain. The patients are extremely grateful for these additions to this field. A very high percentage of them did not request or require a hypodermic of morphine or other narcotic for the relief of pain, although the order for such was left to be used freely as desired. No complication or untoward sequella has been encountered to date in a recent series of cases.

CARCINOMA

In presenting the use of electrocoagulation in the treatment of carcinoma of the rectum to either physicians or patients, the advocate of its use should make himself perfectly clear lest any misconception of this form of therapy should occur in the minds of either the physician or the patient.

I feel that surgery, in the form of radical removal of the growth, continues to offer the patient the greatest chance of complete cure. In this respect we are constantly and impressively reminded of the number of individuals who lead an active and economically secure existence following radical removal of the rectum. The attitude toward colostomy is changing, and rightfully so, for a clean functioning colostomy is preferable to a leaking incontinent perineal anus. Especially is this true when, in the light of surgical experience, abdominal extirpation of a malignant lesion is preferable to incomplete perineal excision.

Although the status of radiation therapy in the treatment of carcinoma of the rectum and pelvic colon is constantly changing there still remains certain inherent difficulties incident to the treatment of malignancy in this region by either X-ray or radium. The selection of cases for radiation therapy must be determined by the physical condition and age of the patient, the size and location of the cancer, the grade of malignancy and its radiosensitivity, the structures invaded and the extent of metastasis. In return, the results may be evaluated upon these same principles and, in addition, in terms of duration of life and comfort of the patient. That there are some cases of malignancy of the rectum that are better off without either surgery, X-ray or radium is attested by the experiences of men like Binkley of Memorial Hospital in New York, Lockhart-Mummery of London, and others. A recent report by Daland on 100 untreated cases of rectal cancer is interesting in this same respect and you are respectfully referred to this interesting paper. The visualization of any malignant lesion of the rectum and pelvis should be accompanied by biopsy and the lesion should be graded, if possible, according to the method of Broders. While the radiosensitivity or radioresistant nature of a neoplasm, as determined in this way, is not an infallible guide to treatment, it does give us some basis for our future management of the case. Further discussion of the grading of malignancy belongs to the field of pathology and will be omitted for the sake of brevity.

Electrocoagulation has considerable to offer certain selected cases as we know that cancer cells are sensitive to heat. It is of value in treating malignant lesions in the aged and inoperable patients that now constitute the large group for whom nothing except an uncared-for colostomy is performed. Many individuals with other physical impairments contraindicating radical removal of the growth may be enabled to spend their days in comparative comfort without the performance of a colostomy. The ideal that is hoped for in the conservative proper use of electrocoagulation is that properly selected cases, especially malignancies of grades 1 and 2, may retain the use of their anus until death from metastasis or some intercurrent disorder supervenes. It is possible to remove a considerable portion of the lesion invading the lumen of the bowel which has been producing partial or even complete obstruction by the use of electrocoagulation. In addition, the bloody purulent discharge with its attendant toxicity is greatly improved without any untoward local or systemic reaction sometimes encountered following radiotherapy. This process of "keeping the lumen open" is a useful procedure in the management of certain cases of rectal cancer. I am unable to subscribe either to its enthusiastic use in treating all malignant lesions of the rectum nor to its unjust condemnation by those unfamiliar with this field of therapy. The field of application is not wide; it is best adapted to cancers of grades 1 and 2, and in the light of our present knowledge it should not be extended to include the early operable lesions.

Let us consider the use of electrocoagulation in the elderly patient with an inoperable rectal cancer. The lesion has existed for some time and while obstruction is not imminent, considerable bloating and gaseous distention are present. The patient may be wearing a diaper during the day because his "piles" were bleeding. In addition, the patient may state that toward morning, around 4 or 5 o'clock, it is necessary for him to get up and go to the toilet where considerable mucus and bloody material are passed. Some will even have an involuntary passage in bed. At examination the lesion is found to have involved over two thirds of the circumference of the bowel and the lumen admits a bougie the size of a lead pencil. Biopsy reveals it to be of low grade. This patient is a candidate for a colostomy which will forestall any obstruction and which will also side-track the fecal stream. We are familiar with the decreased toxicity that follows as a result of this procedure. However, a considerable number of these patients will not be relieved of their discharge or their bleeding. Here, I believe that the judicious use of electrocoagulation is of considerable value. The removal of a large necrotic fleshy mass is followed by a decreasing discharge and an improvement in the patient's condition. The individual can be rendered free of his discharge and its attendant toxicity. He no longer wears a diaper and the nocturnal discharge and bleeding stops. The most important feature is that we are able to maintain a patent lumen and to avoid a colostomy in many of these cases until death occurs. Cure is neither attempted nor considered, but rather the maintenance of the normal route of defecation and the alleviation or eradication of some of the distressing symptoms are the aims.

The full value of electrocoagulation in the treatment of carcinoma of the rectum will be determined when sufficient time and experience have elapsed in its use so that it may be compared with other forms of treatment. If we evaluate our results in terms of duration of life and comfort of the patient, then this valuable adjunct in the treatment of rectal cancer should be accorded a definite place among the recognized fields of therapy.

THE ENDOCRINES IN RELATION TO TUMORS WITH SPECIAL REFERENCE TO THE ASCHHEIM-ZONDEK TEST IN TERATOMA TESTIS*†

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Harvey Cushing, in his address as President of the Association for the Study of Internal Secretions, graphically pointed out the great possibilities in navigation of the "uncharted seas" of endocrinology. At the same time he warned against the danger of false interpretation and misuse of the discoveries which might be made. In presenting a few case records which seem to us to indicate some of the steps which are bringing us toward a realization of some of the predictions which he made, we would urge that they be considered with the measure of caution which should mark the application of all newer procedures if they are to prove helpful rather than useless or even harmful.

The pituitary gland, described in many terms signifying its position as the master gland of the endocrine chain, has been looked upon as related to the elaboration and activity of the so-called pituitary-like hormone, prolan. However this relationship may be decided, it is widely accepted that this hormone is a product of, or is associated with actively functioning chorionic tissue. Therefore, where the presence of the hormone is demonstrated, such tissue may be assumed. In the development of the Aschheim-Zondek test as a means of indicating the presence of this product of chorionic tissue in the urine and in the blood stream lies one of the most significant facts in endocrinology, and through its stimulation to discovery and application of biological tests for other hormones it bids fair to prove a most important factor in the study of many phases of the cancer problem.

Moreover, the importance of this and related developments is twofold. First, as has been observed frequently, it has added new significance to the term "early," as concerned with diagnosis and, therefore, with the effective application of therapy to neoplasms. Secondly, the recognition of systemic evidence of the presence of tissue hyperplasia, that is, of a tumor, actual or potential, before such a tumor is locally demonstrable, encourages the hope that some antagonistic substance, an antihormone, if you wish, may be discovered or developed which, when in turn systemically applied, may serve effectively to control, neutralize or eradicate the neoplastic structure responsible for the elaboration of the hormone itself. Perhaps it is fanciful to attempt to defend this idea by reference to the development of the fetus and fetal membrane as comparable to those neoplasms which we designate as "tumors" in our everyday work. It is but a short step to speculation as to the possibility that this same neoplastic process may be terminated, quite in accord with natural laws by the operation of a neutralizing antihormone, bringing about cessation of fetal development, delivery of the child and restoration of the maternal structures to their former normal condition. And yet this thought has been entertained, at least in an incipient form, by more than one worker (Lindsay, and Harris). It has led us to inject the blood of recently delivered mothers into several cancer patients. In reckoning with the possibility that such a procedure might be worthy of trial, we have had in mind especially the fact that those neoplasms in which the relatively well-understood endocrine product associated with pregnancy, namely, prolan, appears as a common factor, would be the most appropriate ones in which to attempt to produce the possible antagonistic effect of the suggested antihormone to which we have referred. When we speak of a hormone as relatively well understood, we have in mind, particularly, the identity of certain basic radicals common to the formulae of some of the important biologically demonstrable members of this group and to the members of a group of chemical substances recognized for their carcinogenic properties (Murray). Our interest in the material we are outlining is centered in the feeling that it represents in many respects a background, viewed against which a few points at least may assume greater importance than is generally allotted to them from the standpoint of diagnosis, continuous clinical study, and even permissible speculation with regard to tumors. This brief outline is offered with the hope that it may enlarge the use of the Aschheim-Zondek test in the study of problems in this field to which it seems clearly related.

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In pregnancy and those neoplastic processes associated with pregnancy, namely, hydatidiform mole and chorionepithelioma, the concentration of prolan in the urine and blood is high and may be demonstrated by relatively gross tests, as the Friedman test and the Aschheim-Zondek test with unconcentrated urine. On the other hand, the small amount of the hormone present in the case of teratoma testis requires, as a rule, the use of concentrated urine in mice. In any case, we are confirmed in our belief that the curve indicating variations in the amount of prolan from time to time, rather than the absolute amount at any one time, must be our guide in the evaluation of the examination.

Intensive study is being carried on which will doubtless clear up much of the doubt which has been expressed as to the effect of irradiation of tumors with regard to the interpretation of the Aschheim-Zondek test. While the views in this respect as well as with reference to the lower concentrations of prolan in connection with teratoma testis have been somewhat modified by a number of observers, including Ferguson, and Dean, we are convinced that our data justify the conclusions which we present and which we illustrate by the following case records.

We have divided the following reports of cases into 2 groups. The 3 cases in Group 1 impressed us with the value of the Aschheim-Zondek test in the recognition of pregnancy in instances in which tumors introduce confusing factors in the clinical picture and in differentiating between tumors and pregnancy when the latter may be simulated in the presence of the former.

In the second group of 3 cases we have been impressed, not only with the usefulness of the Aschheim-Zondek test in assisting in the diagnosis of teratoma testis, but particularly with the apparent close correlation of the test with the advance and regression of the neoplastic process, a correlation offering aid in the evaluation of therapy and in anticipating the recurrence of neoplastic activity before the actual tumor is recognizable.

REPORT OF CASES

GROUP 1

Case 1: The patient, A. L., a white woman, aged 32 years, was admitted to the hospital on December 9, 1934, with a complaint of dysmenorrhea and irregular menstruation. This had begun in September with severe cramplike pains during the period, followed by unusual soreness in the right side of the abdomen. The history otherwise was irrelevant. On physical examination there was found some tenderness in the right lower quadrant of the abdomen, but no masses were made out. Pelvic examination was not recorded. The patient was operated upon on December 10, 1934, when a panhysterectomy, left salpingo-oophorectomy, and appendectomy were done. The uterus contained several small fibroid tumors and was generally somewhat enlarged. On opening the uterus, a fetus about 7 cm. long was exposed. The postoperative course was uneventful and the patient was discharged, well, on December 23, 1934. The uterus was sent to the laboratory for routine gross examination, the pregnancy not having been recognized. No Aschheim-Zondek test had been made in this case.

Case 2: K. H., a negress, aged 33 years, was admitted to the hospital on the service of Dr. H. P. Ramsey on October 24, 1934, complaining of a mass in the abdomen and dysmenorrhea. The mass had been noted since 1932. Menstrual periods had caused increasingly severe pains, and during the year before admission had not only become irregular, but had increased from 4 to 6 days. Clots were observed especially during the first 2 days. The patient was frequently weak and dizzy after the periods. She was menstruating on admission to the hospital. On physical examination the abdomen was found to be "dome-shaped" and a mass was palpated rising from the pelvis to within 5 cm. of the level of the umbilicus. The cervix was soft, partially effaced, and patulous. The impression was that there was a fibroid uterus, possibly complicating an early pregnancy. X-ray examination on November 20, 1934, revealed a tumor mass extending from the pelvis to the level of the third lumbar vertebra. No fetal bones were demonstrable. An Aschheim-Zondek test the following day was negative for pregnancy. Following the report of this test the abdomen was explored, and although no evidence of pregnancy was found in the ovary, the enlarged, soft uterus was considered by the surgeon to be pregnant, and the incision was closed without further operation. X-ray examination on November 28, 1934, again failed to reveal fetal bones. Two successive Aschheim-Zondek tests with unconcentrated urine were then made and both proved to be negative. A third test with concentrated urine was also negative. On December 3, the abdomen was again opened and supravaginal hysterectomy performed. Several fibroids were embedded in the wall and a large fibroid was found to be suspended from the fundus within and distending the cavity. The uterus did not contain a fetus. The patient recovered after a somewhat stormy convalescence.

Case 3: B. W., a colored woman, aged 41 years, entered the hospital on October 31, 1934, on the service of Dr. H. P. Ramsey, complaining of "swelling" of the abdomen. The family history was unimportant except that her father had died of "dropsy" and her mother had died following miscarriage. The patient's previous history was irrelevant. There had been no pregnancies. The present illness had begun about 15 years before admission, at which time she noticed a "knot on the womb." This had steadily enlarged. The periods had been regular until August 14, 1934, that being the date of the last menstruation. There had been epigastric discomfort and urinary frequency. On physical examination there was found a freely movable mass, quite indurated, filling the lower abdomen and extending to the level 5 cm. above the umbilicus. Bimanual examination revealed a soft cervix, considered characteristic of that of the pregnant uterus. There was a small fibroid posteriorly and to the left, within and obstructing the cervix. The abdominal mass described above was continuous with the uterus. The impression was of uterine fibroids with pregnancy. Aschheim-Zondek test on November 1, 1934, was positive for pregnancy. Hysterectomy was done on November 7, 1934, and a well-developed fetus was found lying between the small fibroid within the cervix and the mass of fibroids making up the tumor felt on examination of the abdomen. The patient was discharged, well, on November 21, 1934.

GROUP 2

Case 4: The patient, S. F., a white man, aged 50 years, first noticed a small tumor involving the left testicle in October, 1934, which had been increasing in size. On December 21, 1934, the Aschheim-Zondek test, with concentrated urine, was positive. On January 3, 1935, Dr. C. P. Howze removed the testicle with the tumor, which was found to be a typical teratoma testis on histological examination. The vas deferens and spermatic cord were cut and tied through the inguinal wound. A few firm nodules were palpable along the vas. In the latter part of January, 1935, a small nodule was palpated in the left scrotum. This grew rapidly until it reached a diameter of about 1 cm. It was considered to represent a recurrence of the tumor. A course of irradiation totaling 3,600 r. (Thoraeus filter) was immediately given, divided between anterior and posterior pelvic areas; 500 r. were also applied to the scrotum. On February 11, 1935, examination showed that the nodule had regressed, and the Aschheim-Zondek test was negative. Two weeks later, only what was considered to be a fibrous nodule could be found at the site of the "recurrent" growth. A small furuncle shortly appeared on the surface of the left scrotum, and an additional 500 r. (½ mm. cu.) was given because of the possibility that the new lesion might be a second recurrence. The infectious nature of the process was clear, however, by its course. An Aschheim-Zondek test was again negative on June 2, 1935. The patient was "feeling fine and gaining in weight." On January 11, 1936, the Aschheim-Zondek test was again negative. On August 4, 1936, however, repetition of the test indicated a slight increase in output of prolan, as compared with the previous negative tests. The patient was still in excellent condition, and early repetition of the Aschheim-Zondek test and frequent observation were urged.

Case 5: The patient, G. H., a white man, 34 years of age, was referred by Drs. F. A. Reuter and E. A. Merritt for an Aschheim-Zondek test on October 25, 1934. A small tumor had been removed with the right testicle on January 10, 1934. Preoperative and postoperative irradiation had been given. Dr. R. M. Choisser, pathologist of the George Washington University Hospital, had reported the tumor to be "seminoma-embryonal carcinoma." A positive Aschheim-Zondek test on April 20, 1934, and a negative test on July 7, 1934, had been obtained with unconcentrated urine. Concentrated urine produced a positive Aschheim-Zondek test on October 25, 1934. Although no tumor could be found, either on examination of the abdomen, or in the groin, or in the remaining testicle, in view of the fact that Dr. Reuter had reported palpating a definite tumor mass in the epigastrium a short time before, 5,600 r. (½ mm. cu.) was given and 14.3 cc. "carcoid" were injected during the period from November 2 to December 5, 1934. An Aschheim-Zondek test on January 24, 1934, in which concentrated urine was used, was negative. On May 9, 1934, the patient appeared well and reported that he was working hard, and no evidence of neoplasm could be found. His weight was 155 pounds. On July 17, 1935, he reported feeling well, but an enlarged lymph node was found in the left supraclavicular region, evidently a metastatic lesion. X-ray examination of the chest showed a large tumor projecting from both sides of the mediastinum just above the heart. Aschheim-Zondek test with concentrated urine, was now positive. The tumor rapidly disappeared under intensive irradiation, no evidence of it being present on examination, including x-ray study, on November 15, 1934. Aschheim-Zondek test on the same date was negative. Until February, 1936, there had been no evidence of a recurrence of the neoplasm, and the patient continued well. When he returned on March 23, 1936, however, a definite abdominal tumor was found. Although this receded under irradiation, and the general condition improved somewhat, the clinical course soon became unfavorable and death occurred, probably with cerebral metastases, on July 7, 1936. No necropsy was permitted.

Case 6: In early 1926, the patient, T. E. D., a white man, 41 years of age, had had the right testicle with a neoplasm removed by Dr. F. R. Hagner. The diagnosis at that time had been "Malignant—probably round-cell sarcoma." The sections were reëxamined in 1934 and reported to represent "embryonal carcinoma." The patient was given irradiation posteriorly in 1926, 600 ma. min. at 50 cm. with $\frac{1}{2}$ cu. each to the anterior and posterior pelvic regions, totaling 1,200 ma. minutes. He remained well until April, 1932, when he was seen by Drs. T. A. Groover and F. R. Hagner, because of the presence of a swelling in the left lateral and anterior regions of the neck, just above the clavicle. No palapble mass could be found elsewhere. X-ray examination of the chest showed the tumor described to be continuous with a growth extending below the sternal notch. A total irradiation of 1,500 ma. min. at 70 cm., $\frac{1}{2}$ cu., 1 mm. al., divided between anterior, posterior and lateral doses was given. By May 26, 1932, the swelling in the region of the neck had disappeared and x-ray examination of the chest showed clear lung fields. Aschheim-Zondek test, performed with concentrated urine, had been positive in April, 1932, but when repeated in May, 6 or 8 weeks later, was negative, coincident with the clearing up of the evidence of the neoplastic process. Examination in July, 1936, was entirely negative, but on November 3, the same year, a mass "about the size of an orange" was palpated in the abdomen, just above the umbilicus. Irradiation of 700 ma. minutes at 70 cm., $\frac{1}{2}$ cu., 1 mm. al., was directed to the tumor anteriorly and posteriorly. Aschheim-Zondek test was positive in January, 1933, and another course of irradiation, 1,000 r., was given anteriorly and posteriorly to the pelvis (total 2,000 r.). On February 15, 1933, the Aschheim-Zondek test was "weakly positive." Although the tumor could no longer be palpated on examination on March 8 nor March 24, 1933, the Aschheim-Zondek test was again positive on the latter date. An additional 1,000 r. was accordingly given anteriorly and posteriorly to the pelvis (total 2,000 r.). Aschheim-Zondek test was again positive on May 20, 1933. The weight had increased, however, and no tumors could be found. In August, 1933, there was still no evidence of tumor and the Aschheim-Zondek test was negative. In May, 1935, 21 months later, while the clinical condition was excellent, the Aschheim-Zondek test was again positive. No treatment was given at this time and the patient did not return for test until April, 1936, when another positive result was obtained. It was found that he had had a cough with expectoration of blood and particles of tissue during the previous 2 months. Examination of the material expectorated showed conclusive evidence of malignant epithelial cells. The patient had lost 5 pounds and an x-ray film revealed an area of opacity in the left apex extending down to the first interspace. A total of 2,500 r. each to the anterior and posterior regions of the left apex was given. On April 23, 1936, marked regression had taken place in the pulmonary growth, and by July, 1936, 3 months later, it had completely disappeared. In the meantime, also, the general physical condition had returned to normal, with a gain in weight. No further Aschheim-Zondek tests have been made at this time.

CONCLUSIONS

1. The Aschheim-Zondek test is worthy of more frequent use in the study of tumors.

2. Its value depends upon a realization of its limitations.

3. Its usefulness will be enhanced by its application before any treatment is undertaken, as well as afterwards.

4. The Aschheim-Zondek test, like all other procedures which may be classed as among the methods of precision, should not be considered as a substitute for, but rather as a stimulus to the most careful study of the history, the physical condition, and the clinical course of the patients concerned.

NOTE: We wish to acknowledge the courtesy of the attending physicians named in the respective case reports and Drs. Groover, Christie and Merritt, who have referred their patients to us and permitted us to present them. We also desire to thank Dr. H. T. Langston, resident pathologist, Garfield Memorial Hospital, for his assistance in analyzing and preparing the material.

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A Review of Eclampsia at the Medical College of Virginia Hospitals.
Summary and Conclusions—(1) A study of our records reveals 105 cases of eclampsia in 5,183 obstetrical cases at the Medical College of Virginia Hospitals, an incidence of 2.02 per cent.

(2) Sixteen maternal deaths occurred, giving an uncorrected maternal mortality of 15.23 per cent. In 1931 and 1932, the mortality rate was 25.53 per cent. In 1933, 1934 and 1935 the mortality rate was 6.88 per cent.

(3) Seventeen babies were stillborn, and 6 newborn babies died, a total of 23, or 23.92 per cent. Therefore, we discharged alive 76.08 per cent of the babies.

(4) Classifying the cases in accordance with Peckham's criteria of severity, it was found that 56.19 per cent of our cases were in the severe group.

(5) A simplified treatment of eclampsia is outlined.

(6) The value of digitalis, magnesium sulphate solution, intravenously in limited amounts and generous amounts of intravenous dextrose solution have been emphasized in our treatment.

(7) We believe that morpbine therapy definitely increases fetal mortality.

(8) In a limited number of selected cases, cesarean section under local or spinal anesthesia may be the operation of choice.

(9) A study of our case records impresses one with the dangers of general anesthesia in eclamptic patients.

(10) The advantages of conservative treatment and non-interference have been discussed.

Extract from paper by H. HUDNALL WARE, JR., M.D., AND FRANCES E. NOBLIN, M.D., Richmond, Va., *Southern Medical Journal, February,* 1937, p. 153.

CALCIFIED HYDROCELE

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A white man, aged 45 years, gave a history of gonorrhea 20 years ago at which time prostatitis, right epididymitis and stricture followed in the way of complications. Since that time the patient has noticed a hard mass almost stonelike in character and weight slowly increasing in size in the right scrotum. The mass is painless unless allowed to hang down unsupported, at which time there is a dull dragging ache radiating down the right groin. He has complete symptomatic relief when wearing a suspensory. The blood Wassermann reaction is negative. The patient has refused further investigation and has no complaints at the present time. With the aid of the roentgenogram shown the diagnosis is calcification of a right hydrocele sac (Fig. 1).

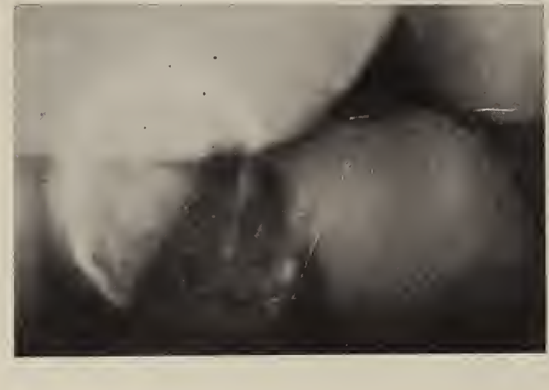

Fig. 1. Calcified Hydrocele

Other cases have been reported as follows: In the patient, 23 years old, operated on by Toulson there was hyalinization of a hydrocele sac; he states that inflammatory masses of great chronicity in and about the testis may undergo hyalinization and give rise to a mistaken diagnosis of new growth. Hyalin tissue is rather common in the pleura, pericardium and spleen but is rare in testis. Hyalinization of a hydrocele is a stage in chronic inflammation and prone to result in calcification.

Bilateral calcification of hydrocele sacs was found at necropsy in a man 72 years old who died of apoplexy. The reporter, Matheson, states they were found on routine examination during life. On section the walls were thickened and showed extensive calcification. The thick contents were greenish yellow, contained cholesterol, and had exerted much pressure on each testis.

Such calcification may accompany new growth, tuberculosis, or syphilis of the testicle. Exploration is, therefore, advisable.

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Further Studies in Vinyl Ether (Vinethene) Obstetrical Anesthesia: Mixtures with Ethyl Ether: Effect on Coagulation Time of Blood . . . . Vinyl ether is a relatively new anesthetic. That it possesses anesthetic properties was first demonstrated by Leake and Chen in 1930. Then, when a pure product had been prepared by Ruigh and Major, Leake, Knoefel, and Guedel found vinyl ether to be preferable to chloroform and ethyl ether. They declared that dogs are more easily anesthetized, that recovery takes place more quickly, that nausea and vomiting are less marked, and that there are no significant pathological effects on the various organs. And then, Gelfan and Bell tried vinyl ether upon themselves and recommended it as worthy of clinical test. A little later extensive experimental and clinical studies were conducted by Goldschmidt, Ravdin, Lucke, Muller, Johnston, and Ruigh; these showed, among other things, liver necrosis in some dogs after prolonged vinyl ether anesthesia, but no liver necrosis in monkeys, as well as no untoward effects on respiration, the circulation, the liver or the kidneys after several hundred operations of a very varied nature on patients of all ages and conditions. . . . .

Summary—First. Vinyl ether anesthesia sufficient for obstetrical procedures is not followed by liver damage. (2) Vinethene does not depress muscle tonus in the intestines and uterus. (3) Vinyl ether anesthesia does not effect changes in the coagulation time of the blood. (4) Vinyl ether may be mixed advantageously with ethyl ether, the portioning of 25 and 75 parts, respectively, is recommended. (5) Vinethene is particularly suitable for obstetrical analgesia and anesthesia in general practice on account of its safety for mother and child, its ease of administration, the rapidity of its action, the satisfactory maintenance of any desired degree of narcosis, and the early uneventful recovery. (6) Although vinethene may be given with relative safety by the "open drop" method, its administration with oxygen in a closed system is very much more desirable.

Extract from paper by Wesley Bourne, M.D., F.I.C.A., J. F. McDowell, M.D., and J. C. Whyte, M.D., Montreal, Canada, *Current Researches in Anesthesia & Analgesia, January-February*, 1937, p. 46.

ABSTRACTS OF PAPERS READ BEFORE THE SOCIETY

"The Insulin Shock Treatment of Schizophrenic Patients,"* **Solomon Katzenelbogen, M.D.**, Henry Phipps Psychiatric Clinic, Baltimore, and **Herbert Harms, M.D.**, Spring Grove State Hospital, Catonsville, Md.

The originator of the insulin shock therapy, Dr. Sakel in Vienna, distinguishes 4 phases in the course of treatment.

First, one tries to determine the patient's sensitivity to insulin and the amount of the drug needed to provoke so-called hypoglycemic or shock reactions. The initial dose, from 12 to 25 units given before breakfast, is gradually increased until marked reactions develop. Four hours after the insulin injection the patient receives 200 to 400 grams of glucose with tea or milk and his regular meal. This preparatory phase of treatment lasts from 8 to 10 days; it may be prolonged up to 3 weeks.

In the second, the most essential therapeutic phase, the dose of insulin varies, the extreme limits so far observed being 25 and around 250 units. The shock reactions, according to their severity, are allowed to last from 15 minutes to 2 hours. They are terminated by glucose. In case of menacing symptoms adrenalin is added. The injections of insulin are given 4 or 5 times a week. The duration of this phase of treatment is between 3 weeks and 2½ months.

The third phase is the rest period, free from insulin for a few days.

Fourth, in case of improvement, one continues with daily injections of insulin, from 10 to 30 units, until the patient's discharge. In this phase, which is the phase of consolidation of the therapeutic benefit, marked reactions are to be avoided. No longer than 2 hours after the injection the effect of insulin is counteracted by glucose.

The most conspicuous reactions commonly observed during the active phase of the treatment are profuse perspiration, excessive salivation, motor restlessness, tremors, clonic contractions, paresthesias, occasionally hemiplegia lasting from a few minutes to several hours, and the most serious reactions, that is, epileptoid convulsions and coma. Convulsions indicate immediate termination of the shock by giving glucose and adrenalin.

The therapeutic effects obtained by Sakel in Vienna and Müller in Switzerland are remarkable. In the treatment of 58 acute cases of less than 6 months' duration Sakel observed in 88 per cent what he calls occupation remission and in 77.7 per cent complete remission. In 46 old cases he obtained occupation remission in 47.8 per cent and complete remission in 19.6 per cent. In Müller's group of 34 cases of 6 months' duration full remission was observed in 76 per cent, and in 51 cases of 1½ years' duration full remission was seen in 68 per cent.

The experience of the Phipps Psychiatric Clinic and the Spring Grove State Hospital can be illustrated by a brief outline of the outstanding facts observed in the treatment of 3 patients.

The first patient is 60 years old, hospitalized for 14 years. The main clinical features all these years were mutism, uncoöperativeness, apparent disinterest in the environment, marked cataleptic reactions. He received the insulin treatment for 2½ months. He strongly reacted to 25 units of insulin, with profuse perspiration, salivation and semicomatose state or deep coma. The points of interest in this case were the hypersensitivity to insulin, as shown by the very pronounced clinical reactions and the low blood sugar values, which on several occasions were around 20 mg. per cent; the fact that the same dose of insulin given at different times but in the same conditions differently affected the blood sugar, which varied from 60 to 18 mg. per cent; and that immediately after his arousal from shock by intravenous glucose the patient showed fair rapport, including conversation but only for a few minutes. No durable therapeutic effect was obtained.

In the second patient, 16 years old, the duration of the illness before the insulin treatment was 4 months. The outstanding clinical features were delusions of persecution, visual hallucinations, mutism, grimacing, uncooperativeness. He was on insulin treatment for 2½ months. He reacted to the injections of 80 or 90 units with profuse perspiration, marked salivation, moderate motor restlessness, drowsiness, sometimes amounting to stupor. The patient benefited from the treatment; he shows interest in what is going on around him. When talked to, he looks very pleasant and cheerful, answers some questions, and reads aloud when asked to do so. Even when he remains silent he still maintains rapport with the interlocutor, smiling and nodding his head in response to questions. The interesting points in this case were that the relatively high dose of insulin, 80 to 90 units, for the most part provoked a moderate hypoglycemia, around 50 mg. per cent and only on 2 occasions 38 and 20 mg. per cent; that there was no consistent relationship between the level of the glycemia and the clinical reactions; and that a marked improvement was obtained in an acute case of only 4 months' duration.

The third patient is 25 years old. The duration of his illness before the insulin treatment was 7 months. The outstanding clinical features were delusions of being doped, auditory hallucinations, and peculiar somatic sensations. The patient was on insulin treatment for a month. He reacted to 75 or 80 units of insulin with very pronounced motor restlessness, moderate or profuse perspiration, drowsiness, and confusion. Since the completion of the treatment, the patient has shown no abnormal behavior. This remission lasted nearly 3 months. He then began to complain of all sorts of diseases for which he made up names, and of phobias. In this case the points worthy of note are: the good therapeutic effect obtained with treatment of only 1 month's duration; the disproportion between very pronounced clinical reactions and only moderately low blood sugar levels, around 50 mg. per cent; the good therapeutic results associated with moderate hypoglycemia.

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* Presented before the Section on Neurology and Psychiatry, December 3, 1936.

There are certain difficulties and danger attached to the treatment. Patients belonging to the parergastic group, like the average population, include individuals who have an average tolerance toward insulin and those who are hypo- and hypersensitive to the drug. The disconcerting fact is that the hypersensitivity may not manifest itself at the beginning of the treatment but may appear later in the course of treatment. A certain dose of insulin which repeatedly caused no reactions at all suddenly and for no apparent reason provokes very serious reactions. The level of glycemia does not consistently prove to be a valid criterion for the possible occurrence and severity of the so-called hypoglycemic reactions; nor does one know of the existence of any other criterion. Finally, because of the frequent occurrence of very pronounced salivation, aspiration of saliva presents a menace, especially in the comatose state.

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"Some Pitfalls in the Diagnosis of Heart Disease,"* **Samuel A. Levine, M.D.**, Assistant Professor of Medicine, Harvard Medical School; Senior Associate in Medicine, Peter Bent Brigham Hospital; Boston.

At the outset I wish to take this opportunity of thanking the officers and members of your Society and the Washington Heart Association, for the privilege of addressing you. I have spent a busy but very pleasant day and I feel particularly indebted to Dr. Ecker and Dr. Yater for their many kindnesses and the trouble to which I put them.

The recent development in our knowledge concerning heart disease has been disseminated so well throughout the medical profession that, for the most part, treatment is carried out quite satisfactorily. This, however, applies only when a correct diagnosis has already been made. In other words, granted that a patient has congestive heart failure from valvular or hypertensive heart disease, or is a thyrocardiac, he is very apt to receive adequate treatment by most general practitioners. The difficulty that still exists is that diagnosis is not sufficiently accurate. Many patients have heart disease that escapes the attention of the physician and many more have symptoms referable to the circulation which simulate organic disease and are treated for such when the condition is neurogenic or due to some other cause. In this respect emphasis needs to be placed on more thorough and accurate diagnosis.

I shall try to touch rather briefly upon some of the more common or more important diagnostic difficulties that arise in general work, and make a few suggestions that may help in diminishing the frequency of the errors involved. In the diagnosis of organic mitral insufficiency, it is essential that there should be a past history of rheumatic fever or chorea and the presence of a moderately loud apical systolic murmur. At times no such past history of rheumatic infection is available, and caution should be exercised in interpreting a systolic murmur, as it can result from a variety of causes. Amongst these are fever, anemia, hyperthyroidism, emotion, and even tachycardia. Furthermore, dilatation of the heart as a result of hypertensive heart disease or myocardial involvement, acute or chronic, may cause a relative insufficiency of the mitral ring without any structural disease of the valve itself.

The diagnosis of mitral stenosis will frequently depend on the detection of the characteristic mid-diastolic or presystolic apical rumble. In some cases this is quite faint and will be entirely overlooked, unless auscultation is carried out very carefully, or unless one listens at the apex directly after a brief physical effort or with the patient lying in the left lateral position. On the other hand, during acute rheumatic carditis, especially in children, an apical diastolic bruit may be found that will disappear entirely in subsequent years. This probably is the result of a relative mitral stenosis with a dilated left ventricle and need not represent a true organic change in the valve.

Aortic stenosis is much more common than one is led to believe from recent teaching. The presence of a loud systolic murmur at the aortic area or over the mid-precordium especially in the absence of hypertension should make one search carefully for a systolic thrill. The latter may be faint and often will become more prominent if palpation is carried out with the patient sitting up and during a forced expiration. Furthermore, calcification of the aortic valves can often be observed on fluoroscopic examination. Either the presence of a basal systolic thrill or calcification on X-ray examination is practically certain evidence of aortic stenosis.

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*Presented before the joint meeting of the Washington Heart Association and the Society, December 9, 1936.

As a result of the great advance in our understanding of the clinical aspects of coronary thrombosis, we are now in the situation that this diagnosis is made too often in cases where some other mechanism is the cause of the chest pain or distress. Some of the other conditions that simulate acute coronary thrombosis are pulmonary embolism, pneumonia, acute dissecting aneurism of the aorta, acute pneumonothorax, spondylitis, herpes zoster, lung tumor, etc. These and other conditions will need to be considered at various times in differential diagnosis, when the possibility of coronary thrombosis comes to one's mind. Many conditions produce some alterations in the ventricular complexes of the electrocardiograms, and although the latter may be of extreme diagnostic value, minor changes require very cautious interpretation.

Because the small group of masked thyrocardiacs are so responsive to proper treatment, it is imperative that we should ever be alert to detect this factor of hyperthyroidism amongst our patients suffering from heart disease. Almost all of these cases do show evidence of an independent and ordinary type of heart disease, such as hypertensive heart disease, coronary artery disease or rheumatic valvular disease. But they are suffering, in addition, from the increased burden of a hyperthyroid state which can be eradicated. They will not show exophthalmos or thyroid enlargement and because of this, they go undetected. Careful search for and interpretation of minor features will be necessary, such as undue loss of weight, sweating, tremor, diarrhea, feeling of warmth, hyperactive heart sounds, transient auricular fibrillation and failure of a rapid irregular heart rate to slow on adequate digitalis administration. These and other peculiarities should lead one to make basal metabolic studies which also require critical interpretation, because heart failure itself may cause some elevation in the metabolism. Finally the response to iodine therapy may be diagnostic.

A common error in general practice is the misinterpretation of the significance of dyspnea. Breathlessness is the most important symptom of heart failure, but because it is a manifestation of other diseases, it often is difficult to properly appraise its mechanism. It is commonly the result of asthmatic bronchitis, or emphysema, and incorrectly regarded as due to organic heart disease. In the former, the râles are apt to be generalized, coarse or sibilant with prolonged expiration, whereas in the latter they are moist and often confined to the bases of the lungs. The treatment and prognosis are also quite different in the two conditions. Furthermore, dyspnea may often be due to simple obesity without any heart disease. Here again, digitalis will be useless or harmful, and the prognosis is excellent. Finally, there is a form of breathlessness that occurs as a purely neurotic or functional manifestation and is often accompanied by a peculiar sighing type of breathing. All these conditions need to be carefully distinguished from organic heart disease, because of the striking differences in therapy and prognosis involved.

Probably the most important and most frequent diagnostic mistakes are in the group having functional or non-organic types of cardiovascular disorders. Most of the irregularities of the heart can occur without structural disease of the heart. Many patients have insignificant systolic murmurs and should not be regarded as cardiac cripples. Then there is the group of cardiac neuroses and neurocirculatory asthenia that must not be confused with structural disease. In all these functional conditions, once he has convinced himself of the true situation, the physician should speak to his patient with assurance, decision and optimism, for only in that way will rehabilitation be obtained and cardiopathophobia be prevented.

Chronic Diffuse Glomerular Nephritis. .... Chronic nephritis has been regarded as a disease whose signs and symptoms depend upon the pathology of the kidney. The treatment of this condition has consequently been carried out with the dominant idea of sparing the kidney as epitomized in the German expression "Schonungstherapie." The method consisted principally in rest, a low protein (lacto-vegetarian) diet, and residence in a warm dry climate. These therapeutic measures accomplished little, but were the best available..... Permanent bed rest is satisfactory for a few months in acute nephritis, but carried on indefinitely for chronic nephritis will result in disuse atrophy of the muscular and glandular tissues; a low protein diet lessens the excretory demands upon the kidney but results, *first*, in tissue deterioration including the kidney itself, *second*, in the early development of anemia, and *third*, in a susceptibility to infectious diseases, notably tuberculosis; residence in warm dry climates uproots the patient—children cannot attend school, men cannot follow their occupations and women leave a struggling household behind them; furthermore, hotel or boarding house life at its best is associated with discomforts and inconveniences which favor colds and infections that can be much more readily avoided by suitable clothing and shelter in a wintry climate with routine family fireside care.....

....A high protein diet will not damage the kidney but will tend to preserve the integrity of the whole organism. Some of the peoples of India who are strict vegetarians are prone to suffer with nephritis. The minimal quantity of protein in the diet regarded as satisfactory according to Peters is 75 grams plus the quantity of albumin lost in the urine; larger amounts have been advocated but are not necessary.....

The edema of diffuse glomerular nephritis is of three varieties:

1. The toxins of the hemolytic streptococcus, in acute glomerular nephritis or in acute exacerbations of chronic diffuse glomerular nephritis, damage the capillaries and increase their permeability to the contained blood.

2. Cardiac insufficiency which, as is generally appreciated, may result from prolonged hypertension in chronic diffuse glomerular nephritis, will bring about a type of edema similar to that produced by the failing heart under any circumstances.

3. A lowering of the blood proteins especially the albumin, is accompanied by a diminished osmotic tension in the blood and an escape of fluid into the tissues from the circulation. This is a characteristic symptom in the so-called nephroses; it may also occur in the course of chronic diffuse glomerular nephritis when it is regarded as a nephrotic component of the nephritis.....

Summary—The treatment of chronic nephritis today recognizes the fact that this disease of the kidneys is made up of several elements which demand individual attention. These are: the lesion of the kidney itself, that is the nephritis; edema; hypertension; impairment of renal function; malnutrition and anemia; uremia. These phases of nephritis are not only treated when they arrive, but the administration of drugs and diet should attempt to anticipate their appearance. All treatment, especially dietetic therapy, is aimed to maintain the patient in good physical condition and to make no attempt to deny the body necessary nutrition because of efforts at shielding the kidney which are now recognized as being of no value; stress is put upon the idea of feeding a sufficient quantity of foods with a high protein content, especially meats, which do not injure the kidney, alleviate edema, do not cause a rise in blood pressure, prevent malnutrition and anemia, and need only be curtailed when a considerable degree of impairment or renal function makes its appearance. In other words, a high protein diet can be used for the treatment of every phase of chronic diffuse glomerular nephritis except when retention uremia is threatening.

Extract from article by HERMAN O. MOSENTHAL, M.D., New York City, *New York State Journal of Medicine, February* 1, 1937, p. 268.

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MANDELIC ACID—A NEW URINARY ANTISEPTIC

The introduction of mandelic acid as a urinary antiseptic is the culmination of an orderly progression of scientific investigations made during the last 4 years by American and English urologists. With its development there has been evolved a more rational basis for the treatment of the infections of the urinary tract.

Clinical experience has long recognized that acidification of the urine seems to have a deterrent influence on the growth of the colon bacillus. Shohl and Janney[1] had shown that the growth of Escherichia coli was inhibited in urine at a pH 5.0 or lower, but in practice it is very difficult to maintain this degree of acidity by drugs alone. In 1931, Clark,[2] and Helmholtz,[3] working independently on the observation that the urine of patients on the ketogenic diet was highly acid, found that such urine was also definitely bactericidal. This led them to undertake a study of the value of the ketogenic diet in the treatment of colon bacillus infections, and the success they achieved has firmly established this form of therapy. Helmholz[4] in the following year was able to demonstrate that the destructive action of ketone urine is due to a bacteriostatic substance and not to acidity.

Fuller,[5] by chemical fractionation, identified this bacteriostatic substance as beta-hydroxybutyric acid and found that this acid exercised in vitro a strong bacteriostatic action below pH 5.5. Attempts to replace the ketogenic diet by the oral administration of beta-hydroxybutyric acid were abandoned when it was found that the acid was completely oxidized to carbon dioxide and water in the body under normal metabolic conditions.

After experimenting with similar organic acids, Rosenheim,[6] in 1935, found that mandelic acid exerted a bacteriostatic action in vitro equal to that of beta-hydroxybutyric acid; moreover, when taken by mouth it is nontoxic and is excreted unchanged in the urine in sufficient concentration for bacteriostatic action, provided the pH of the urine is lowered to 5.5. He administered this acid to 15 patients with infections of the urinary tract with good effect.

A series of experiments was conducted by Helmholz and Osterberg[7] to determine the concentration of mandelic acid and the pH necessary for the urine to possess bactericidal activity against the organisms commonly invading the urinary tract. These organisms are largely bacillary in type, including Escherichia coli, Aerobacter aerogenes, Proteus and Pseudomonas. Staphylococcus aureus and albus, Streptococcus faecalis and a green-producing streptococcus, and organisms of the genus Micrococcus are next in frequency.

The common bacilli are killed by a 0.5 per cent concentration of mandelic acid at a pH of 5.3. With proper care, it is possible to maintain a 1 per cent concentration of the acid at a pH of 5.0 for many days.

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[1] Shohl, A. T., and Janney, J. H.: The Growth of Bacillus Coli in Urine at Varying Hydrogen Ion Concentrations. J. Urol., 1917, **1**, 211.

[2] Clark, A. L.: Escherichia Coli Bacilluria Under Ketogenic Treatment. Proc. Staff Meet., Mayo Clin., 1931, **6**, 605.

[3] Helmolz, H. F.: The Ketogenic Diet in the Treatment of Pyuria of Children with Anomalies of the Urinary Tract. Proc. Staff Meet., Mayo Clin., 1931, **6**, 609.

[4] Helmolz, H. F.: The Ketogenic Diet in the Treatment of Urinary Infections of Childhood. J. A. M. A., 1932, **99**, 1,305.

[5] Fuller, A. T.: Ketogenic Diet; Nature of Bactericidal Agent. Lancet, 1933, **1**, 855.

[6] Rosenheim, M. L.: Mandelic Acid in the Treatment of Urinary Infections. Lancet, 1935, **1**, 1,032.

[7] Helmholz, H. F., and Osterberg, A. E.: Rate of Excretion and Bactericidal Power of Mandelic Acid in the Urine. J. A. M. A., 1936, **107**, 1,794.

Escherichia coli and Proteus ammoniae are easily killed, and certain strains of Aerobacter and Pseudomonas also; but the greater number of strains of Aerobacter and Pseudomonas can only be killed by higher concentrations of bactericidal action. This can be obtained by decreasing the pH level or increasing the concentration of the mandelic acid. It is important to know that Proteus ammoniae produces a strongly alkaline urine, so that it is very difficult to attain the proper pH at which it can easily be destroyed. A few strains of staphylococcus have been tested and seem to correspond in vulnerability to the bacillary organisms, but the action of mandelic acid on the coccus organisms has not been adequately studied. No favorable clinical results have attended the use of mandelic acid in the treatment of coccal infections in adults, but in children it has been used satisfactorily in both coccal and bacillary types of infection. Two cases of Streptococcus faecalis infections have been cured.

Clinical experience with this drug has been brief but very encouraging. In most cases the urine becomes sterile within 4 to 12 days, regardless of the duration of the infections. Careful administration and supervision are essential for successful treatment. Fluids are restricted to 1,200 cc. daily. The diet must be free of alkali. Mandelic acid is best given in the form of its ammonium salt, a powerful acidifying agent in itself. The dose is 12 grams daily (Elixir Ammonium Mandelate, 1 tablespoonful 4 times daily). The urine should be tested daily and additional ammonium nitrate or other acidifying measures given if found necessary to maintain the urinary pH below 5.3. The urine, if sufficiently acid, will give a pink color upon the addition of methyl red.

Rosenheim,[8] and Cook and Buchtel,[9] have had the largest clinical experience with this drug. Rosenheim treated 88 unselected cases of acute and chronic infections of the urinary tract caused by the bacillus coli, reporting 63 per cent cured. Cook and Buchtel reported a series of 75 patients treated with sodium mandelate and the urine of 61 of them, or 81 per cent, was rendered sterile. Failures or recurrence could generally be explained by inability to properly acidify the urine, by the presence of foci of infection within or without the urinary tract, or by the presence of urinary obstruction and stasis. Rosenheim has stated that any case under proper management which does not result in sterilization of the urine after 2 weeks should have a thorough urologic investigation for one of the above complications.

Contraindications to the use of this drug include the presence of renal insufficiency. In such cases sufficient concentration of the drug cannot be excreted by the kidney, so that a bactericidal action is not produced and symptoms of acidosis may develop. There is some question as to the advisability of its use in the acute febrile state of the infection because of the necessity of limiting the fluid intake. The risk involved may be minimized by the thoroughness of the medical supervision. Undesirable side effects include nausea and vomiting (1 per cent of cases), diarrhea (10 per cent of cases), hematuria (4 cases) and a temporary decrease in renal function. There is no evidence that mandelic acid can produce permanent renal damage.

It is obvious that any attempt to submit a critical appraisal of the value of this new urinary antiseptic would be premature at this time. The brilliant clinical results obtained so far are confirmation of the sound laboratory data that produced it. Its limitations are very definite so that many of its failures can be predicted. Mandelic acid is not a panacea but promises to be a very valuable adjunct in treatment of certain infections of the urinary tract.

M. J. McI.

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[8] ROSENHEIM, M. L.: Mandelic Acid in the Treatment of Urinary Infections. Lancet, 1936, 2, 1,083.

[9] COOK, E. N., AND BUCHTEL, H. A.: Mandelic Acid in the Treatment of Infections of the Urinary Tract. J. A. M. A., 1936, 107, 1,799.

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS

The regular meeting of the Washington Society of Pathologists was called to order at 1:30 P.M., January 9, 1937, in the Army Medical Museum by the President, Dr. Roger M. Choisser. The minutes of the previous meeting of December 3, 1936, were read by the Secretary, Captain Elbert DeCoursey, and approved.

Scientific Paper

"Giant-cell Tumor of Bone." **Janvier W. Lindsay, M.D.**, Garfield Memorial Hospital.

Ambroise Paré recognized that giant-cell tumors of the jaw could be cured by repeated excision. The benign character of giant-cell tumor of bones has frequently been emphasized since that time, but probably largely as the result of the continued use of the word "sarcoma" the condition has been treated as a malignant disease and subjected to radical surgery.

Bloodgood (1920) proposed the substitution of "benign giant-cell tumor" for "giant-cell sarcoma." It is now generally agreed that the great majority of giant-cell tumors of bone are benign. It is not agreed that they are true neoplasms. The problem of change of a benign into a malignant form of giant-cell tumor to osteitis fibrosa cystica and hyperparathyroidism are still under discussion. Ewing noted an instance of what he believes to be the development of a giant-cell tumor from the wall of a cyst in osteitis. In the last edition of his "Neoplastic Diseases," he uses the term "osteoclastoma" for this pathological process.

The determination of the benign or malignant character of the giant-cell tumor rests on certain accepted features of location, X-ray findings and biopsy. In connection with their study, the determination of calcium and phosphorus in the blood, particularly since hyperparathyroidism has become so much emphasized in recent years, has been considered an important diagnostic and prognostic feature. The phosphatase content of the blood probably offers more useful data than the phosphorus and it is evident that isolated determinations of the blood calcium are not necessarily helpful. The estimation of the metabolism of calcium represents an elaborate procedure. The ivory wedges proposed by Stain of Philadelphia seem likely to be valuable and simple aids in connection with these problems in that they show graphically the deposit in or removal from the bones of these substances.

The matter of treatment has been much discussed, and the various procedures are familiar to all.

Dr. E. A. Merritt and his associates were, I believe, the first to apply irradiation to the parathyroids in the attempt to control and cure benign giant-cell tumors, being led in this step by their belief that these pathological processes represent a phase or type of hyperparathyroidism.

We shall present lantern slides of several cases which we have classified as benign tumor, recognizing that some features, such as location and appearance of the stroma with variable numbers of mitotic figures and extensive arrangement, like development, leave the possibility of malignant change still to be reckoned with.

Discussion

Captain Elbert DeCoursey: This microscopic slide is from a 22-year old white man who gave the perfect history of a benign giant-cell tumor; also the x-ray picture showed a perfect benign giant-cell tumor, and it was so diagnosed. In New York City there are several men, particularly at The Memorial Hospital, who do not operate on benign giant-cell tumors, do not make biopsies, but make the diagnosis by the x-rays, treat it by x-rays, and cure it by x-rays. This man was so treated for 15 months and he received 1,500 r. but the tumor suddenly started getting out of bounds and an amputation was necessary. As you saw in the microscope, there were some giant cells. (By the way, this tumor at first was also diagnosed by a needle being stuck into the tumor and a few cells being taken out.) Although there were giant cells and an x-ray picture of a perfect giant-cell tumor, metastases in the lung and death followed within 8 months after the amputation. From the histologic picture of the amputated tumor one hesitates to decide between malignant giant-cell tumor and osteogenic sarcoma as the correct diagnosis. A regular biopsy at first would presumably have shown a malignant picture also.

Dr. Lester Neuman: I am not particularly in favor of punch biopsies but in giant-cell tumor there is an opportunity for making a punch biopsy if all of the other evidence, especially the x-ray evidence, points more or less definitely to a benign giant-cell tumor. We have on a number of occasions been able to remove plasma and tissue with a large needle and a tight syringe and make very satisfactory diagnoses of these so-called benign giant-cell tumors, one of which I showed to the Society 3 or 4 years ago. I believe that if there is an indication for punch biopsy, this is probably one of the best.

Dr. R. M. Choisser: We see very few giant-cell tumors on our service, but those that do come in offer frequently a great deal of confusion. The majority of true giant-cell tumors at biopsy show a typical benign type of histology. The fact that giant cells are present in a tumor, however, does not indicate, of course, that such tumors are of benign nature, and I feel that all of these tumors arising from the bone showing giant cells, whether they are roentgenologically negative or not, should be looked at with suspicion.

Dr. Lindsay, in closing: While the ordinary criteria for diagnosing benign or giant-cell tumors are supposed to be very simple there is really considerable confusion. Some of these cases have raised the question as to whether they are truly benign or malignant. The last patient I mentioned is just recovering from her operation, so it is too short a time to tell definitely what the results will be. Dr. Neuman referred to the matter of punch biopsies. I also am not in favor of punch biopsies as a routine practice except for those positive findings which we may get; if we have a negative result we are probably not much better off that we were before; but if we are fortunate enough to get a positive result we have information of great value. The second case which I showed was presented for that reason. In the second case there was some definite indication that irradiation of the parathyroid produced deposits of calcium in the bone. One of the important things, as Dr. Matz has indicated, is to get away from the use of the term "sarcoma" in reference to the benign giant-cell tumor; in other words, cease calling them benign giant-cell sarcomas. There is very definite evidence that the irradiation of the parathyroids does stimulate the deposit of calcium in the bones.

Some of these cases of osteitis and similar conditions may recover without any treatment whatever; while that is rare, it must be reckoned with. It is also important that enough calcium be supplied in the blood either by diet, medication, or any other method to assure an adequate supply for its deposit in the bone.

Presentation of Cases

Dr. C. H. Binford presented a case of a white man, aged 73 years, whose chief complaint was nocturia, frequent passing of gravel for 1 year, and burning sensation during and following urination. The clinical diagnosis was benign hypertrophy of the prostate with retention of urine and acute uremia, and calculi of the prostate and urethra. The principal gross pathologic diagnosis was calculi of the bladder and urethra; gangrenous cystitis with gangrenous and infected suprapubic postoperative wound; gangrene of the penis; atrophic cirrhosis of the liver; chronic splenitis. The principal histopathologic diagnosis was mucous papillary adenoepithelioma of the bladder; gangrenous urethritis, penile; chronic pyelitis and pyelonephritis, slight; acute splenitis; arteriosclerosis, general; portal cirrhosis, early.

Dr. L. L. Ashburn presented the case of a white man, aged 45 years, who gave a history of 6 months' illness with diarrhea, bloody and mucoid stools. There was no tenderness, poor appetite, and some nausea and vomiting. Several X-ray pictures (presumably of the gastro-intestinal tract) were negative. He lost 40 pounds in the last 6 months. R. B. C., 3,370,000; hemoglobin, 11.1 Gm.; W. B. C., 20,350, poly's 76 per cent, lymphocytes 21 per cent; transitionals 3 per cent. A biopsy of the ulcer of the rectum was submitted for examination with a tentative diagnosis of carcinoma of the rectum or ulcerative colitis.

Dr. Ashburn presented a second case of a white man, aged 59 years, who was admitted to the hospital, December, 1936, stating that 3 years before he had had acute retention of urine with cystitis and enlarged prostate. The prostate was removed at that time. He frequently has passed large masses of what appeared to be necrotic tissue. At operation a hard nodular tumor of the bladder was found in the region of the trigon. The tumor showed much surface necrosis and a few polypoid projections of masses of varying size. This is considered a case of leiomyosarcoma.

In the discussion opinions were mostly in agreement with leiomyosarcoma. The question of the picture being a sarcomatoid reaction in an anaplastic carcinoma was considered.

Dr. Ashburn presented a third case of a white man, aged 65 years, who stated that he had received a direct blow in the left axillary region, after which enlargement of the lymph glands in this region had occurred. The glands enlarged in 3 months to a globular mass about 6 inches in its longest diameter. The clinical impression was lymphadenitis or lymphosarcoma. The histologic diagnosis was metastatic melanotic nevocarcinoma. The tumor mass (fixed) was demonstrated.

Dr. R. J. Jermstad presented a case of a white man, aged 60 years, who had had a biopsy from a lymph node from the neck 15 years ago. The diagnosis was Hodgkin's disease. He had received x-ray treatment. There was no further clinical recurrence. He developed hypertension 2 years ago. A series of cerebral accidents followed, finally resulting in death. At autopsy the spleen was enlarged (weight 375 Gm.) and contained several firm tumor nodules, which histologically proved to be Hodgkin's disease. No evidence of the disease was found elsewhere in the body.

Dr. Lester Neuman presented several slides from a tumor of a 39-year old woman, multiparous, who had been examined regularly and in whom no tumor had been found 3 years before. She had a large mass in the pelvis which the surgeon believed to be an ovarian cyst; but upon operation he found a large, encapsulated tumor, lightly attached to the bladder but definitely attached to the omentum; it was also connected with unusually large blood vessels. There were no other evidences of such masses in the abdominal cavity. The ovary, tubes and uterus were all normal. The tumor on the cut surface was pale yellow and more or less lobulated, and gave somewhat the appearance of a placenta except for the yellow color; the large blood vessels running around one side looked almost like an umbilical cord. It evidently is a hemangioma, but the question is whether or not it might not be a hemangiosarcoma. The stroma is extremely cellular.

In the discussion it was noted that the region of the broad ligament is prone to increased cellularity in the presence of lesions. That the process was benign seemed to be the consensus of opinion.

Captain Elbert DeCoursey presented microscopic slides from a tumor from the orbit of a 19-year old colored man. The tumor was about 3 cm. in diameter and clinically was making the eye pop out of the head so that the ophthalmologist thought surely it was a tumor. In the Masson stain there were some large clear cells, some of which have red granules only, others have granules plus a few small red rods, and in others the rods are lined up forming fibrils; others are frankly fibrillar and have cross striations. These cells, one may say, may be degenerative pure muscle cells or they may be myoblasts. With the tremendous amount of muscle present, it is more than extra-ocular muscle tissue. The Masson stain demonstrates anaplastic cells with cross striations. It is probably one of those rare rhabdomyosarcomas of the orbit.

Dr. R. M. Choisser presented a case of a 34-year old woman who had worn a stem pessary for 4 years without removal. Her menstrual periods during this time had been regular. She removed the pessary on the advice of a physician and became pregnant soon thereafter. She aborted in the sixth week and was curetted (specimen No. 1) for excessive bleeding 3 days later. Specimen No. 2 shows curettings 6 weeks later. The Aschheim-Zondek test was negative. It is thought the process is benign, but there is a question of chorioepithelioma.

In the discussion it was considered that this picture was that of an unusually exaggerated normal reaction to pregnancy.

The meeting adjourned at 3:20 P.M.

COMING MEETINGS

Friday, February 19: *The Section on Ophthalmology and Otolaryngology.*

1. "A Trip With the President." Captain Ross T. McIntire, M.C., U.S.N.
2. "Case of Streptococcus Throat; Clinical and Postmortem Report." Allan E. Walker, Jr., M.D.
3. "Laryngeal Tumors—Bronchogenic Tumors with their Bronchoscopic Diagnosis." Chevalier Jackson, Jr., M.D., of Philadelphia.

Wednesday, March 4: Stated Meeting of the Society. Election of members of Nominating Committee which will select nominees for various elective offices of the Society for the year 1937–1938; election of new members; reports of officers and committees, etc.

Wednesday, March 10: Joint meeting with the Section on Ophthalmology and Otolaryngology. E. Ross Faulkner, M.D., of New York City, will be the invited speaker, and will address the meeting on "Sinusitis."

Wednesday, March 17:

1. "Syphilis in a Medical Clinic." George W. Creswell, M.D.
2. "For All Our Sakes." (Motion picture.) Under the auspices of the Washington Council of Social Agencies. Discussion by William A. White, M.D.
3. "Summary of Local Plans for the Venereal Disease Problem in the District of Columbia." George C. Ruhland, M.D.

Wednesday, March 24: Joint meeting with the Section on Neurology and Psychiatry.

Wednesday, March 31:

1. "Hypogastric Sympathectomy." Joseph J. Mundell, M.D.
2. "Treatment of Intussusception in Children." Crenshaw D. Briggs, M.D.

NEWS AND PERSONALS

George W. Calver, Captain, Medical Corps, United States Navy, an Associate Member of the Medical Society of the District of Columbia, had his address, "The Man Past the Forties," which was read before the Mayo Clinic Staff, October, 1936, published in full in the Milwaukee Medical Times, January, 1937. He gave an interesting digest of methods employed in his daily professional activities in the keeping of members of Congress well.

Dr. Arthur C. Christie's paper, "Present Conception of Radiation in Treatment of Cancer," which was read before the Eighty-fifth Annual Session of the Iowa State Medical Society, appears in full in the January issue of the Journal of the Iowa State Medical Society, pages 1–9.

Dr. Norman P. Scala, and Dr. E. Spiegel (by invitation), read a paper, "The Cortical Innervation of Ocular Movements," before the Philadelphia Neurological Society at its stated meeting held January 22, 1937, in the auditorium of the College of Physicians, Philadelphia.

Dr. Lewis H. Taylor was recently elected president of Sibley Memorial Hospital by the Board of Trustees of the Woman's Home Missionary Society which conducts the institution. Dr. Taylor was graduated from the George Washington University School of Medicine in 1903; and has been a member of the Medical Society of the District of Columbia since April 5, 1905. He is past president of the American Therapeutic Society and chairman of its Council for a number of years; also a past president of the University Club. The Visiting Staff of Sibley Memorial Hospital, through the chairmanship of Dr. Joseph F. Elward, is arranging a testimonial dinner to be given Dr. Taylor at the Mayflower Hotel on March 1.

Fifth Annual Postgraduate Clinic, George Washington University School of Medicine, will be held Saturday, February 20, 1937. On this date there will be opportunity for hearing prepared papers, attending clinics and viewing work now in process in the various laboratories. An invitation is extended to all alumni, members of the George Washington University Medical Society and the profession generally to attend. The annual banquet of the George Washington University Medical Society will be held at the Mayflower Hotel on the evening of February 20. Dr. Cyrus Cressey Sturgis, Professor of Internal Medicine, University of Michigan, Ann Arbor, will be the guest speaker.

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The Smith-Reed-Russell Lecture was held in the George Washington University School of Medicine, February 11, 1937. The guest speaker was Dr. Harvey B. Stone, Associate Professor of Surgery, Johns Hopkins University; his subject, "Acute Intestinal Obstruction."

ANNUAL SCIENTIFIC ASSEMBLY

May 5–6, 1937

The General Committee, Dr. Joseph Horgan, Chairman, in addition to placing on the program outstanding teachers from the two medical schools and specialists in practice in Washington, will make full use of the peculiar advantages that the Nation's Capital has in Government laboratories and hospitals. Among these stand notably the National Institute of Health, the United States Army Medical Center, Mount Alto Hospital, and the National Academy of Sciences. If emphasis is to be placed on any particular phase of practice it will be on treatment. The objective will be to render in the postgraduate presentations the more practical aspects of therapy. Available for those interested will be a setup of the Washington Plan for the distribution of medical care.

Dr. James Clarke White Will Address Meeting

Inclusive with out-of-town speakers will be Dr. James Clarke White, who will give a summary of the never advances in surgery of the sympathetic nervous system. Dr. White was graduated from Harvard University School of Medicine; is a Fellow of the American College of Surgeons, and member of the American Society for Clinical Investigation. He is Assistant Professor of Surgery in his alma mater.

Tri-state Conjoint Meeting

On Wednesday, May 5, will be celebrated the second annual Tri-state Conjoint Meeting. There are no registration fees. To all who register Wednesday, A.M., will be issued complimentary tickets to the Mayflower Hotel Luncheon. The banquet is to be held on Thursday evening. Remember these dates. Formal program will be available early in March. Secure your copy.

Thomas Linville, M.D.

CAT.

(1874-1936)

Dr. Thomas Linville, who practiced in Washington since 1904 and who at one time was an Associate in Medicine on the faculty of George Washington University School of Medicine, died suddenly on February 1, 1937. He was born in Winston-Salem, N. C., and it was there he received his preliminary education. His degree in medicine was obtained in 1904 from the George Washington University School of Medicine. In 1909 he was elected a member of the Medical Association of the District of Columbia. He served the Society faithfully on many committees, among which are noted the Building Committee, the Legal Advisory Committee, and the Periodic Health Examination Committee. He frequently contributed scientific papers to societies of which he was a member. His last paper read before the Society was "Banti's Disease; Case Report." He served on the staffs of George Washington University Hospital and Children's Hospital. For years he served the public school system on the Medical Inspection Staff. In his society memberships are included the Clinical Club of Washington, the George Washington University Medical Society and the American Medical Association.

Dr. Linville is survived by his wife, Clara Merriam Linville; a daughter, Mrs. J. Robert Talbott of Syracuse, N. Y.; two sons, Thomas Merriam Linville of Schenectady, and Gilbert Winston Linville of New York City; and his mother, Mrs. Cornelia A. Linville of Winston-Salem.

The funeral was held on the afternoon of February 3. The following members of the Society acted as honorary pallbearers: Drs. Charles W. Hyde, Charles S. White, S. L. Battles, C. W. Culver, Henry A. Polkinhorn, F. J. Eichenlaub and Frank Leech.

BOOK REVIEW

Toxicology or the Effects of Poisons, by Frank P. Underhill, Ph.D., thoroughly revised by Theodore Koppanyi, Ph.D Philadelphia, P. Blakiston's Son & Co., 1936; Third Edition, 325 pages. Price: $2.50.

This toxicology was compiled by the late Professor Underhill of Yale University in 1924 for the purpose of presenting the effects of poisons on the organism in a concise manner, which would appeal to both the student

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and the physician and yet be comprehensive enough to enable them to obtain a clear concept of the essentials underlying the subject.

Since its origin it has been revised but once by the original author. Many advances have been made in this science since Professor Underhill's death in 1932, necessitating a rather radical revision of many subjects and the addition of others. This task was assigned to Professor Koppanyi of Georgetown University, who has brought the book in line with present-day concepts of action and treatment.

In its revision Professor Koppanyi has retained not only the form but the original text so far as possible. Among the new substances described therein are the newer barbiturates, camphor substitutes, cinchophen and its derivative neocinchophen, cyclopropane, dinitrophenol, ephedrine, mercurial diuretics, quinine substitutes, thyroid, tri-brom-ethyl alcohol, and tri-orthocresyl phosphate. The sections on carbon tetrachloride, thymol, thallium and food poisoning have been rewritten.

Neither the isolation nor the chemical identification of the individual poisons has been considered, apparently in the effort to make the work concise. In previous editions treatment was outlined rather than given in detail. This idea has been departed from somewhat and more extended details of treatment are given for a number of substances.

Underhill's Toxicology has been of much service to both student and physician since its origin. It has become a standard text-book on the subject and since this edition has been satisfactorily revised and does not radically depart from the intent of the original author, it should continue to occupy a high position among the texts intended as guides to this important subject.

G. B. R.

MEDICAL SOCIETIES WITH LIMITED MEMBERSHIP
1937

WASHINGTON, D. C.

SOCIETY	PRESIDENT	SECRETARY	REGULAR MEETING
Academy of Medicine of Washington	William A. White	Errett C. Albritton	Quarterly
Baltimore-Washington Dermatological	L. Ginsburg, Balto.	F. A. Ellis, Balto.	3d Thursday
Clinical Club	R. L. Sexton	Harry S. Bernton	1st Tuesday
Clinico-Pathological	Matthew W. Perry	Lee McCarthy	1st and 3d Tuesdays
George Washington University	W. Raymond Thomas	Harry F. Dowling	3d Saturday
Georgetown Clinical	Joseph J. McHale	Harry F. Davies	3d Tuesday
Hippocrates-Galen	P. A. McLendon	H. L. Darner	1st Thursday
International Medical Club	Tomas Cajigas	P. S. Constantinople	On Call
Jacobi	Alec Horwitz	Samuel A. Machlis	3d Monday
Kober	Howard L. Smith	William M. Ballinger	3d Monday
Mackall	Richard W. Wilkinson	M. W. Glover	3d Thursday
Medical Arts	Walter R. Stokes	J. Ogle Warfield, Jr	2d Thursday
Medical Review Club	G. R. Huffman	John F. Preston	4th Friday
Osler	John H. Lyons	Walter Atkinson	3d Monday
Pan American (D. C. Branch)	Henri de Bayle	A. A. Moll	On Call
Virginia, Maryland and District of Columbia	B. C. Perry	A. Magruder MacDonald	Semiannually
Washington Academy of Surgery	Charles S. White	W. Warren Sager	2d Friday, Bimonthly
Washington-Baltimore Psychoanalytic	Lewis B. Hill, Balto.	Amanda L. Stoughton	2d Saturday
Washington Gynecological	Prentiss Willson	Herbert P. Ramsey	4th Saturday*
Washington Heart†	James W. Esler	B. W. Leonard	Quarterly
Washington Medical and Surgical	J. Duerson Stout	Robert Oden	4th Monday
Washington Ophthalmological	James N. Greear, Jr.	Ernest Sheppard	1st Monday, Bimonthly
Washington Society of Nervous and Mental Diseases	Samuel A. Silk	William G. Cushard	3d Thursday
Washington Society of Pathologists	Roger M. Choisser	Elbert DeCoursey	1st Saturday
Washington Urological	S. R. Coleman	Ivy A. Pelzman	Monday‡
Women's Medical	Anna Bartsch-Dunne	Elizabeth Parker	1st Tuesday

* October, November, January, March and May.

† Permanent office with lay secretary, Mrs. Wade Martin, 1315 Nineteenth Street, N. W.

‡ Every six weeks, September–May.

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ECTOPIC PREGNANCY: SOME HIGH LIGHTS IN ITS HISTORY

GEORGE J. BRILMYER, M.D.

Associate Professor of Pathology, Georgetown University School of Medicine, and Associate Professor of Biology, Catholic University

The adjective "ectopic" is taken from the Greek; ek meaning "out of," and topos meaning "place." Literally, therefore, an ectopic pregnancy is a pregnancy "out of place," and since the normal place for a pregnancy is within the uterine cavity an ectopic pregnancy may be defined as that condition in which the embedding and growth of the impregnated ovum take place elsewhere than in the uterine cavity. The term "extra-uterine pregnancy" may be used as a synonym for "ectopic pregnancy," meaning that the fertilized ovum may become implanted in the tube, in the ovary, or anywhere on the abdominal peritoneum. When the ovum develops in that part of the tubal canal which is included in the wall of the uterus the condition is then styled an "interstitial" pregnancy. While an interstitial pregnancy is a type of ectopic pregnancy most cases of ectopic gestation occur farther out in the tube proper. Of the tubal variety most take place in the tube's outer half or middle.

While embryos have been found in the lower uterine segment, in the canal of the cervix, and even within the vagina, such cases must more correctly be regarded as forms of abortion rather than true ectopic pregnancies.

Tubal pregnancies tend to occur in the free portion of the tube; as a rule, at about the middle. These cases tend to abort or rupture between the second and fifth months and be extruded into the abdominal cavity. Very rarely does a tubal pregnancy go on to full term unless it grows out between the layers of the broad ligament. It is then styled an intraligamentous tubal pregnancy.

Occasionally a pregnancy occurring in the infundibulum projects itself into the abdominal cavity. Such a condition is called a tubo-abdominal pregnancy. If the fetus is discharged from the tube into the abdominal cavity it is then a tubal abortion. If, however, instead of being discharged into the abdominal cavity through the open end of the tube, the embryo is discharged into the peritoneal cavity through a rupture of the wall of the tube, we then term the condition a tubal rupture. In cases where the fimbriae closely embrace the ovary, or where a tubo-ovarian cyst has existed into which a ripened follicle had ruptured and a fertilized ovum has started development, we speak of it as a tubo-ovarian pregnancy. While true ovarian pregnancy is rare, it has occurred and we shall cite such cases.

Whether or not a pure form of abdominal pregnancy ever exists is still open to question in the minds of many. A more critical examination into cases reported as such reveals that many were primarily tubal or ovarian and had been transplanted (via rupture or abortion) from their original site, for but few convincing cases have been reported. Cases of secondary abdominal pregnancy occur in which the sac ruptures and the fetus is then discharged into the body cavity. In such cases development is possible so long as the placenta remains intact and communication with the mother is maintained.

Strange to say, in ectopic pregnancy the uterus undergoes changes comparable to those occurring in a normal pregnancy. The uterine muscle hypertrophies and a decidual membrane forms. The cervix may even partially dilate and the decidua may in time be cast off. Except for those relatively rare cases of interstitial pregnancy, where delivery may take place in the natural way, the fetus in an ectopic pregnancy invariably dies. If the products of conception are small they may be completely absorbed. Usually, however, when the fetus is discharged into the abdominal cavity it becomes encapsulated and degenerates. Mummification, maceration, or calcareous infiltration (lithopedion formation) may occur. Now and then only the membranes become calcified, and this condition is designated as lithokelyphos.

As regards the safety of the mother, tubal pregnancy is the most dangerous, since rupture of the tube after the earlier months invariably tends to occur. Such tubal rupture may lead to sudden and even fatal hemorrhage. The bleeding may take place freely into the abdominal cavity (hematocele) or the blood may become more or less encapsulated (hematoma).

According to several authorities, Albucasis was the first to describe a case of ectopic pregnancy. Albucasis, whose real name was Abulkasim, was an Arabian by birth. He was a surgeon and lived in Cordova, Spain, in the eleventh century. He observed parts of a fetus escaping through the abdominal wall of a woman. The parts came out through a suppurating sinus and there can be but little doubt that it was a true ectopic pregnancy. This case occurred about the middle of the eleventh century.

In the year 1500, Jacob Nufer, a Swiss swine spayer, performed the first reported operation in a case of ectopic pregnancy. Nufer's patient was his own wife who had been in unsuccessful labor for several days. After 13 midwives and several lithotomists had been attending her and had failed to render her any relief, Nufer realized the gravity of the situation and sensed the condition. He obtained his wife's permission to perform the operation. Next, he had to obtain the permission of the chief magistrate of the village. After much bickering and difficulty this permission was finally granted. Then Nufer asked those with enough courage to remain and assist him with the operation; the others he requested to leave the room. It was not at all strange that 11 of the 13 midwives lost no time in leaving.

After prayer Nufer laid his wife on the table and opened her abdomen with an incision identically the same as he was accustomed to make in the swine. The incision was cleverly and carefully made and the child was safely extracted. When the 11 midwives outside the room heard the extracted child cry they clamored for readmission, but Nufer refused to readmit them until after the incision had been closed and the child had been washed. The incision healed rapidly. Nufer's wife was later confined 4 times, at 1 time bearing twins. She lived to reach the age of 77 years. The child which Nufer delivered by the operation also lived to a ripe old age. The scene of this historic operation was in the quaint little village of Sigerhausen, Switzerland.

Forty years later, in 1540, Christopher Bain operated upon a woman named Lodovica. Bain's operation, no doubt, was for an ectopic pregnancy. In 1594 Primrose performed a similar operation, and in the same century Platerus, Horstius, Polinus, and Cordaeus reported other cases of ectopic gestation. In the case of Cordaeus the fetus had been converted into a lithopedion and was carried in the abdomen for 28 years. Horstius related the history of a woman who in 1547 conceived for the third time, and in 1563 the remains of the fetus were still in the abdomen.

According to J. Clarence Webster, Riolanus the Younger was the first to report a case of tubal pregnancy. This was in the year 1604. In 1614 Mercerus reported the first case of ovarian pregnancy. According to some authorities, Saint Meurice should get joint credit with

Mercerus for describing this first ovarian pregnancy.

Perhaps one of the earliest plates of an extra-uterine pregnancy is that made by Francois Mauriceau in 1669. Mauriceau's description of this extra-uterine pregnancy, although written nearly 300 years ago, is not inferior to some of those presented in our text-books of today. It is an admirable account and runs as follows:

"History of a woman in whose abdomen there was found, after death, a small fetus about $2\frac{1}{2}$ inches long, together with a great quantity of coagulated blood. The history of this case deserves to be carefully examined into to decide whether the fetus (as believed by many) was generated in the ejaculatory vessel, called the tube of the womb.

"On the sixth of January, 1669, in the village of Corrari, I saw in the hands of a chirurgus, called Benedict Vassal, a uterus, the picture of which is shown at the end of this chapter, which the same chirurgus had a short time before removed from the body of a woman, aged 32, who died after 3 whole days of torture with the most agonizing pains in the stomach, through which she had fallen into frequent fainting spells and the most violent convulsions.

"This woman had borne 11 children at term, but in her twelfth pregnancy, at about $2\frac{1}{2}$ months the womb dilated in the direction of the right horn, and unable to stand distention, ruptured. The fetus was cast out at once and found among the intestines of the mother with a great quantity of coagulated blood in the lower abdomen. Many physicians, chirurgi, and other students of nature did as did we ourselves, betook themselves to this chirurgus to see the uterus (which he showed for a prodigy, persuading them that it was formed in the ejaculatory vessel, which Fallopius calls the trumpet of the womb). They believed at once without any more investigation, that this was just as the chirurgus had told them, and that this case confirmed stories of a like nature narrated by Riolanus. However, I examined the parts of that uterus most carefully and attentively, and it was known to me that those who had fallen into this opinion were in the error whither the chirurgus was leading them, and for this reason, at that very time, I took a drawing of the womb as it then was, and this is a more faithful, true drawing than that which the chirurgus caused to be engraved on brass after an entire month, at a time when the uterus retained almost nothing of its primitive form. and was spoiled by the handling of a thousand men or more who had seen the uterus, pulled it, disturbed it, turned it inside out that they might examine it. . . .

"Many have brought forward this case to prove to us that the testes '(ovaries)' of women are full of little ova which at the moment of coitus, freeing themselves and emerging from the body proper of the testes '(ovaries)' are borne into the uterus through the tube afterwards to serve for the generation of the fetus; and 1 of these so-called ova had by chance remained in the tube of this woman, and that this was the cause of her death. Regnus Graaf among others holds this opinion, for the confirmation of which he brings forward the figure of this uterus which he painted from the case which the chirurgus of whom I have spoken, had already given to the public; as one finds it on the two hundred and sixtieth page of his book on the generative organs of women; but any who will, carefully and without prejudice, examine the following figure which is most faithful and faultless and at the same time examine into our reasons, will find that we have given another demonstration and that we believe to be the true explanation." (Translated from the Latin.)

Although Mauriceau gave us such a good description of this case and illustrated it by an excellent figure, he did not believe that it was a true tubal pregnancy. He evidently considered it a hernia from the right horn of the uterus but it was clearly a case of extra-uterine pregnancy. It is open to speculation, however, as to whether it was "tubal" or "interstitial" in type. At any rate, this case started an acrimonious discussion concerning ectopic pregnancy, which discussion has continued for nearly 3 centuries.

The first clear description of "interstitial" pregnancy was made by Dionis in 1718. In

1759 John Bard of New Jersey did a laparotomy for extra-uterine pregnancy. In 1784 Josephi reported the first case of "abdominal" pregnancy. In 1791 William Baynham of Virginia performed a laparotomy for ectopic pregnancy. In 1792 Deutsch published his remarkable work at Halae. Deutsch's work was most noteworthy because of the life-size plates he submitted upon the abdominal form of ectopic pregnancy. In 1799 Baynham did his second laparotomy on a case of ectopic pregnancy. In 1801 Schmitt published his "Beobactung der K. K. Med. Chir.," and in 1816 John King of Edisto Island, South Carolina, delivered the first full-term ectopic fetus via the vaginal route. He cut through the posterior wall of the vagina and applied forceps to the fetus. With abdominal pressure exerted from above and traction from below he successfully delivered the child. Both the mother and the child lived, and in 1818, at Norwich, England, King published his views on ectopic pregnancy in a volume of 176 pages, entitled "An Analysis of the Subject of Extra-uterine Foetation and of the Retroversion of the Gravid Uterus." This was the first book written upon the subject. Ten years later, in 1826, Pfaff of Leipsig brought out his work on interstitial pregnancy wherein he had a series of plates exhibiting the pathology, along with a number of specimens of this type of pregnancy. In 1828 Breschet "rediscovered" the interstitial form of ectopic pregnancy and gave a description of this type in his "Memoirs sur une nouvelle espece de gross extra-uterine." In 1831 J. Guentz wrote a description of the abdominal type of ectopic pregnancy, while Madam LeFort deserves the credit of having been the first to report a case of an ovum developing between the layers of the broad ligament (1836). This case was called "subperitones-pelvic" pregnancy by Dezeimeris in his classical classification of ectopic pregnancies which he published in the same year. In 1848 Gordon spoke of a curious case in a negress, 6 months pregnant, in which an extra-uterine fetus in the cul-de-sac occluded the uterus via compression. The fetus was removed through the vagina. Two days later labor pains set in and in 2 hours the negress was delivered of a uterine child as well. The placenta was left behind, drainage was established through the vagina, and the woman made a complete recovery.

In 1876 John S. Parry of Philadelphia published his book, "Extra-uterine Pregnancy." The book was based upon 500 cases which Parry had collected from the literature, 23 cases of which showed combined "extra-" and "intra-" uterine pregnancies existing at the same time. In 1881 Küchenmeister reported mummification and lithopedion formation, two of the most favorable terminations of advanced extra-uterine pregnancies. In 1883, in Europe, Veit made the first positive diagnosis of an unruptured tubal pregnancy. Three years later Janvrin made the first one in America. On January 17, 1883, Lawson Tait did the first successful operation upon a case of ruptured tubal pregnancy, but Stephen Rogers had suggested such an operation as early as 1867. Loschge, in 1887, was the first to recognize the "subperitoneal" type of ectopic pregnancy. In the same year Werth of Kiel caused the dawn of a new era in the critical examination of specimens when he published at Stuttgart his remarkable work entitled "Beitrage zur Anatomie und zur operativen Behandlung der Extrauterinschwangerschaft."

It was in this same year (1887) that Spiegelberg laid down the 4 conditions which must be fulfilled before one can be certain of an ovarian pregnancy. These conditions are: (1) That the tube on the affected side be intact, (2) that the fetal sac occupy the position of the ovary, (3) that it be connected with the uterus by the ovarian ligament, (4) that definite ovarian tissues be found in its walls. In 1889 Lawson Tait reported 2 cases of ruptured tubal pregnancies; in 1891 B. J. Kouwer described ovarian pregnancy. In that year Landau, Rheinstein, and Williams demonstrated the presence of diverticula from the lumen of the tube and advanced this condition as one cause of tubal pregnancy.

In 1899 von Both reported a most remarkable condition. He had a case of tubal pregnancy which ruptured at 5 months. Upon diagnosis he did a laparotomy, tied off the bleeding points, and closed the abdomen. Three months later he reopened the abdomen and removed the fetus finding it living and attached to the right tube. In the same year (1899) at the Third International Congress of Gynecology and Obstetrics at Amsterdam, Katherine van Tussenbroeck reported a case of ovarian pregnancy. Some authorities maintain that this was the first authentic case reported. In 1902 Opitz showed many specimens in which the tips of the folds of the tubal mucosa had fused together and he advanced this condition as another cause of ectopic pregnancy. In 1908 Norris and Mitchell reported a case of primary ovarian pregnancy. J. Clarence Webster is probably the only one to report 2 such cases (1904) and, strange to say, both cases were in the practice of the same physician in a small Wisconsin town. In 1913 Mall and Cullen reported another unquestionable primary ovarian pregnancy, clearly demonstrating that it was within a graafian follicle.

When an ectopic fetus dies it may go over to lithopedion formation and then be retained within the body cavity for years, or it may undergo maceration and degeneration. If the latter happens fetal bones may later be passed through the body wall of the mother or they may rupture into the intestinal tract and then be passed by rectum. Discharge of the fetal bones or even the whole of an extra-uterine fetus by the rectum has been reported many times but these cases were not as common as the discharge of fetal bones through the abdominal walls.

In the eleventh century Albucasis observed parts of a fetus escaping through a suppurating sinus in the body wall of a woman. In 1668 Margaret Parry of Berkshire passed the bones of a fetus through the body wall above the os pubis. Sixteen years later she was still alive and well and had given birth to several healthy children via normal deliveries. Skippon, in 1731, reported a case of the discharge of fetal bones through an "imposthume" in the groin, while Brodie reported the history of a negress who at about the seventeenth month following conception expelled a fetus from an abscess at her navel. Algora, in 1878, spoke of an abdominal pregnancy in which there was spontaneous perforation of the anterior abdominal parietes, followed by death. In 1884 Bouzal cited an extraordinary case of ectopic pregnancy in which there was expulsion of the fetus through the abdominal wall with subsequent intestinal strangulation. An artificial anus was established and the mother recovered. Campbell quoted the case of a Polish woman, aged 35 years, the mother of 9 children, most of whom were stillborn, who conceived for the tenth time, the gestation being normal up to the lying-in period. Then she had pains followed by extraordinary effusion and some blood into the vagina. After protracted complaints the abdominal tumor became painful and inflamed in the region of the umbilicus. A breach in the abdominal wall soon formed, giving exit to purulent matter and the bones of a fetus. The patient received no medical attention during this process and had but little assistance in dressing the draining sinus. She recovered but had an artificial anus all her life.

In Volume VIII of the Philosophical Transactions of the Royal Society of London there appeared a remarkable report. Sarah McKinna had 2 normal deliveries but in the second month following the birth of her second child she again showed symptoms of pregnancy. At the end of 9 months these symptoms, with the exception of the suppression of the menses, subsided, and she continued in this condition for 6 years. The first 4 years caused discomfort in the umbilical region. About the seventh year she suffered tumefaction of the abdomen, the abscess broke, and an elbow of a fetus protruded from the wound. A butcher enlarged the wound and, hooking his finger under the jaw of the fetus, he extracted the head. Upon looking into the abdomen he observed a black object so he inserted his hand and extracted piecemeal an entire fetal skeleton along with some decomposed animal matter. The abdomen was then bound up and in 6 weeks the woman was able to superintend her domestic affairs. With the exception of a ventral hernia the woman had no bad after-effects.

Kimura, quoted by Whitney in 1893, had an extraordinary pregnancy in a Japanese woman, 41 years of age. In this case an arm protruded through the abdominal wall just above the umbilicus and the remains of a fetus were removed through this opening. Brodie, Dunglison, Erich, Fox, and Wilson are among others reporting the expulsion of parts of ectopic pregnancies through the abdominal parietes.

Discharge of fetal bones or even the entire extra-uterine fetus by the rectum has often occurred. There are 2 early cases mentioned in the Philosophical Transactions of the Royal Society of London in 1748, in which the bones of a fetus were passed at stool, causing intense pain. Armstrong in 1835 described an anomalous pregnancy in a syphilitic patient who discharged fetal bones by the rectum.

Hyerdahl in 1847 spoke of the expulsion of extra-uterine remains after 13 years' retention, and in 1865 Jackson reported the dissection of an extra-uterine sac which communicated freely with the large intestine. In 1870 Peck reported the spontaneous delivery of an extra-uterine fetus by the rectum, with recovery of the mother. Benham, in 1876, mentioned the discharge of a fetus by rectum in a patient who had a rectal stricture associated with syphilitic patches, necessitating the performance of a colotomy. In 1886 Butcher described an ectopic pregnancy delivered through the rectum at the fourth month with recovery of the patient; in the same year Bubendorf reported the elimination of a fetal skeleton by rectum after 5 years' retention with recovery of the patient.

Perhaps the most remarkable case of its kind was that of a 4-month tubal pregnancy, which became adherent to and ruptured into the gut, without any soiling of the peritoneum, the clotted bright red blood being passed by rectum. This case was reported in 1920 by Chase and is mentioned here because of its rarity. In this case no infection was present, the tube simply became adherent to the pendulous, mobile cecum and then ruptured into it secondarily. This case was operated upon 7 hours after admission to the hospital. The abdomen was opened through a mid-line incision. The omentum and several loops of the intestine were adherent to the posterior surface of the right tubal mass. The omentum and 2 loops of the intestine were easily separated, but when the cecum was pulled away, an opening in it the size of a silver dollar was disclosed. This opening was adequately plugged by a blood clot. There was no other rupture and no blood in the cul-de-sac or pelvis. The rent was repaired, the right tube and mass were removed, and a drain of gauze was carried through the vagina from the cul-de-sac. The mass removed consisted of blood clot and tube. A portion of the tubal wall was inflamed, and the blood clot showed a delicate membrane (apparently amnion) and abundant trophoblasts. During the operation the patient was given 500 cc. of 5 per cent glucose solution intravenously, and on the fourth day after the operation a second blood transfusion was given, 500 cc. of blood having been given previous to the operation. The patient gained rapidly and went home on the twenty-first day after the operation. No other case has been found in the literature in which the cecum received the contents of the tube.

In 1932 Clark of Brooklyn reported a case of interstitial pregnancy which had ruptured into the sigmoid. The sigmoid was adherent to the uterus as the result of a previous operation.

In 1933 Mundell reported a case of full-term abdominal pregnancy in which a live baby was obtained and the mother recovered. The placenta was left in situ and the abdomen closed without drainage.

Ectopic pregnancies have even ruptured into the urinary bladder. In 1608 Bartholinus and Rosseus spoke of fetal bones being discharged from the urinary passages. Ebersbach, in the Ephemerides of 1717, described a necropsy in which a fetus was found in the urinary bladder. In 1878 White reported an instance of the discharge of fetal remains through the bladder. The only possible explanation of such instances would be through an ectopic pregnancy rupturing into the urinary bladder after having had its primary seat in a tube or within the abdomen.

The first authentic case of primary abdominal pregnancy was reported by Galabin in 1896.

His case was that of a pregnancy situated in the cul-de-sac. In 1903 Witthauer reported a second case. In Witthauer's case the placental tissue was found in a rolled-up piece of omentum attached to the pelvic organs.

In March, 1904, in the Revista ibero-americana de ciencias médicas, Gutierrez reported the first convincing case of primary abdominal pregnancy. He found in a woman of 34 a mature fetus in a sac in the abdominal cavity. The sac was attached to the great omentum and the parietal peritoneum, the placenta being inserted on the great omentum itself.

Another authentic case of primary abdominal pregnancy was reported by Hirst and Knipe in 1908, in which the fertilized ovum was implanted on the posterior aspect of the left broad ligament.

In June, 1927, in a review of 156,000 cases of pregnancy at the New York Lying-in Hospital, Harrar found 10 cases of apparently primary abdominal pregnancy, but in his opinion all of these were secondary to ruptured tubal pregnancies.

Davis in 1901, Kynoch in 1925, LeDoux in 1926, and Furgason and Scott in 1928, reported cases of primary abdominal pregnancies.

In November, 1931, Best reported a most interesting case of primary abdominal pregnancy in a Russian Jewess, aged 35 years, whose first symptom was an agonizing pain in the lower portion of the back and abdomen with a bearing down sensation in the pelvic region. She had an urgent desire for evacuation of the bowels but was unable to defecate. Repeated enemas only resulted in the return of the enema fluid. Her abdomen was tender over both lower quadrants. The perineum was only slightly relaxed, the posterior vaginal wall was pushed so far forward toward the symphysis by a mass behind it that it was difficult to introduce the examining finger past it. On insertion of a finger into the rectum, a mass the size of a small grapefruit was found bulging into the rectum just about 2 inches above the anus. As the sphincter was markedly relaxed, by slightly retracting it with the fingers a globular, dark, bluish mass was brought into view. A tentative diagnosis of an unusual type of extrauterine pregnancy complicated by hemorrhage was made. Immediate surgical treatment was arranged for. The first plan was to do an immediate laparotomy without interference through the rectum or vagina, but upon repeating the rectal and vaginal examination after spinal anesthesia, the mass bulging into the rectum seemed to be on the point of rupture. Because of this and the desperate condition of the patient, it was thought that a simple puncture and evacuation of the contents of the mass, evidently a blood clot, would be sufficient for the time being. On puncture of the mass through the rectum, a large quantity of blood clot was evacuated followed by a large quantity of blood. The continued flow of blood now deemed a laparotomy imperative. A mass the size of an orange, firmly fixed in the cul-de-sac, could still be felt below and behind the uterus. When the abdomen was opened, a large quantity of fluid and clotted blood was evacuated, after which a placenta and 4-month fetus were uncovered, situated in the cul-de-sac. The placenta was attached to the peritoneum of the floor of the cul-de-sac, the anterior wall of the rectum, and the lower portion of the posterior aspect of the cervix. The fetus and placenta were shelled out, the general peritoneal cavity was sealed off, the space between the uterus and rectum was marsupialized and this space packed with gauze. A large quantity of saline solution by hypodermoclysis was given; then followed a transfusion of 500 cc. of citrated blood. The patient showed marked immediate and sustained improvement and went on to recovery, although it took 47 days for a resultant fecal fistula to heal. Two days later she was discharged from the hospital.

When an ectopic pregnancy coexists with a uterine pregnancy this condition is styled a "combined pregnancy." Many authentic cases of combined pregnancy have been recorded. Chasser, in 1812, spoke of a case in which there was concurrent pregnancy in both the uterus and the fallopian tube. Clark and Ramsbotham, in 1856, reported double conception, 1 fetus being born alive in the normal manner and the other being extra-uterine.

Brown, in 1881, reported 24 such cases of combined pregnancies. Gutzwiller, about 1893, reported 18 cases; Martin, 1895, published 6 cases; Strauss, in 1898, was able to collect 38 cases, all of which occurred between 1820–1898; Zinke reported 71 cases (1902); and in 1903 Bichat wrote concerning 49 cases. In 1905 Weibel had increased the number to 119, while in 1913 Neugebauer added many more cases to the list.

Twin tubal pregnancies have also been observed. While they are rare they have been found with both embryos in the same tube as well as with 1 in each tube. Hardouin, in 1919, collected 36 cases where the embryos were in the same tube. Arey believes that single ovum twins occur more often in tubal than in uterine pregnancies. Sänger, Krusen, and Diamant have reported cases of triplets in tubal pregnancy.

In 1895 Ahlfeld reported a case of tubal pregnancy in a 17-year old girl, Margaret D. This case was complicated with sarcoma of the uterus, the tubal pregnancy at first being overlooked.

In 1913 Doederlein and Herzog reported a case of ectopic pregnancy in an adenomyomatous uterus. The patient, Mrs. K., aged 37 years, had a mass in her left parametrium. The mass was about the size of a 4 to 5 months' fetus. The uterus itself was empty and not enlarged but the mass proved to be an adenomyoma. Opening the mass, a placenta was found in a state of good preservation. The embryo had previously been expelled.

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THE USE OF PREGL'S SOLUTION IN THE TREATMENT OF OCULAR INFECTIONS*

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This paper on the use of Pregl's solution was prepared after personal experience with 60 cases of ocular disease covering a period of 2 years. The use of this solution is not new, a previous article on the same subject having been published by Cowan in the Archives of Ophthalmology, March, 1930. Cowan also read a paper on this subject before the Medical Society of the State of Pennsylvania in October, 1934.

Pregl's iodine solution is an amber fluid prepared in 1 cc. ampules. This is advantageous, not only because this is the average dose of this drug, but because Pregl's iodine solution degenerates quite rapidly when it comes in contact with air. Any deviation from the amber color is an evidence of deterioration, and the solution should not be used.

Pregl's iodine solution is a complex hypoiodite compound, which, as it comes in contact with any weakly acid medium, liberates nascent iodine. The weakly acid medium is practically always found in any inflammatory condition of the tissues. The freeing of iodine in the tissues, combined with its action as a lymphagogue, and the production of a local chemotactic irritation is of benefit in many of the conditions for which this solution may be used. Pregl's iodine solution aids in checking progress of corneal opacification. Regardless of the primary condition, injections of Pregl's solution retard, from their earliest use, a growing opacity of the cornea. It has been found to be most useful, therefore, in those diseases in which opacities of the cornea are the sequelae most to be feared. Often the effect on the cornea is almost immediate, and in many cases a decided change for the better can be seen in 12 hours.

It is interesting to note also, in passing, that Pregl's iodine is used intravenously after mastoidectomy or following a sinus operation when there is a septic rise in temperature or suspicion of septicemia. After administering Pregl's solution in these cases it is the rule for the temperature to change from a septic type to one of a steadier character.

The ocular conditions for which Pregl's solution is indicated are all infectious forms of keratitis or kerato-iritis with the possible exception of dendritic keratitis, but particularly severe ulcerative keratitis with hypopyon. The cases treated and forming the basis of this report were extremely variable in regard to the extent and intensity of the ocular infections; later, 2 illustrative cases will be described in which Pregl's solution was administered.

Technic

The original technic of Pregl therapy described by Cowan has undergone a beneficial modification. His original technic was to thoroughly irrigate the conjunctival sac with sterile boric acid or normal salt solution and then to instill several drops of holocaine hydrochloride. After anesthesia thus had been obtained, 15 minims of Pregl's solution was slowly injected under the bulbar conjunctiva as near the limbus as possible and as close to the chief area of corneal involvement as possible. If the conjunctiva happened to be chemotic, the highest point of the edema was chosen for the site of injection. Immediately after the injection, iced compresses were applied to the eye, because severe ocular pain usually followed. Jordan attempted to abolish this severe reaction by adding to the 15 minims of Pregl's solution in the syringe 2 minims of holocaine, but it was found that the combination of these drugs resulted in a cloudy solution, and possibly some chemical change in Pregl's solution, the nature of which has not been determined.

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* Read before the Ophthalmological Section of the Baltimore City Medical Society, December 3, 1936.

After various experiments a newer technic was evolved, and this is the one in vogue at present. The conjunctival sac is thoroughly flushed with mercurophen (1 to 8,000 solution) and then cocaine (4 per cent solution) or holocaine (2 per cent solution) is instilled at the rate of 2 drops at 2-minute intervals until 5 instillations have been given. Then 5 minims of novocaine (2 per cent solution) is injected subconjunctivally, and a few minutes are allowed to elapse for anesthetization of the tissues and for abatement of the chemosis arising therefrom. One cc. of Pregl's solution is then administered subconjunctivally, and this is followed immediately by iced compresses which usually are required continuously for half an hour before there is absolute freedom from discomfort. In this manner the severe pain experienced with the older technic is markedly alleviated, the reaction depending, of course, on the general make-up of the patient. Pregl's iodine is usually administered every other day, but in severe infections is given daily until there is a distinct improvement noticed. Then it is given on alternate days. In addition to Pregl therapy it is necessary to use atropine (1 per cent solution), and usually local hot applications for 20-minute periods every 2 hours. General measures, such as foreign protein injections, mercurial inunctions of 1 dram on alternate days, and medication such as salicylates combined with soda, or quinine, are also desirable.

Illustrative Cases

Case 1: J. Y., 43 years of age, entered the hospital on September 26, 1934, for the removal of a cataract of the right eye. Examination of the right eye showed that the pupil was fixed and could not be dilated by the usual preoperative use of atropine. Slit-lamp examination showed the iris structure to be slightly atrophic and several posterior synechiae. The lens showed the presence of a uveal cataract. As is the custom, the eyes were cultured for organisms preoperatively. On September 27 and again the next day, 24-hour and 48-hour cultures showed long-chain streptococci present from the right eye. The use of argyrol (20 per cent)—1 drop followed in 10 minutes by a mercurophen (1 to 8,000 solution) flush every 2 hours—was instituted for the cultured eye. On October 3 the culture of the right eye was negative, and a simple intracapsular extraction followed by peripheral iridectomy was done. On the occasion of the first dressing 2 days later, examination revealed the cornea to be quite hazy with marked exudate and hypopyon in the anterior chamber. There was also a marked chemosis of the conjunctiva. It was evident to the observer that a severe postoperative infection was already active. Treatment with Pregl's solution was instituted and continued for 5 days along with hot salt compresses for 15 minutes 3 times a day, atropine (1 per cent solution) twice a day, mercury rubs of 1 dram on alternate days, and mercurophen flushes 4 times a day. During the first 3 days of this treatment no change was noted in the eye under observation, and it was evident that the infection was being held in abeyance by the treatment. On the fourth and fifth days after the use of Pregl's solution, the luster of the cornea appeared to be improving, and there was some lessening of the hypopyon. Chemosis of the conjunctiva was still quite marked, but the patient stated that he could see the light held by the examiner much more clearly than he could on the second day. The pupillary opening was covered entirely with the exudate which had earlier almost filled the anterior chamber. The pupil still remained undilated. The usual postoperative atropine had been used, and extra measures to cause dilation were used, such as atropine and adrenalin packs, and Gifford's subconjunctival injection of adrenalin, atropine, and cocaine. There was no increase in intra-ocular tension nor did it occur at any time.

The condition improved rapidly after the fifth day, when the last Pregl's solution of the 5 consecutive treatments was given. From this time on the patient received 3 additional treatments of Pregl's solution on alternate days. The inflammatory condition of the eye and the chemosis of the conjunctiva subsided rapidly after October 9 (sixth day), and the patient was discharged from the hospital on October 19 with a quiet eye, to return later for an iridocapsulotomy. A visual test on his departure revealed good light perception and projection and hand movements at 1 meter. On November 19 the patient returned to the hospital, and examination of the eye previously treated showed the cornea clear with the exception of a scar "at 12 o'clock" from the previous cataract extraction. The iris structure appeared good although slightly lighter in color than the left iris, and there was a complete occlusion of the pupil by organized exudate. The vision was the same as at the time of discharge.

After the customary preoperative culture which was negative, an iridocapsulotomy was done with a resulting moderate-sized central opening. The eye remained quiet following this operative procedure and at no time showed any signs of an exacerbation of the acute process which followed the previous surgical interference. Three days after the operation the patient was discharged with 1 per cent atropine instillations twice a day and advised to return to the clinic in a week. The patient returned again on December 5, at which time examination of the right eye showed the cornea to be slightly hazy, the anterior chamber somewhat cloudy, and a few strands of capsule present over the pupillary opening which was 3 mm. in diameter. There was a slight injection of the bulbar conjunctiva. Slit lamp showed some interstitial haziness of the cornea with some deep vessels appearing from the region of the superior limbus. There were marked keratic precipitates on Descemet's membrane and some disintegration of the endothelium. The anterior chamber contained many cells and showed vitreous extending through the pupillary opening and intermingling with the aqueous. There were many large floating vitreous opacities. On refraction, a 6/100 vision was obtained with a plus 13 sphere. It was thought inadvisable to give the patient any correction at this time but to continue treatment and recheck his refraction about 6 weeks later. The patient returned in 2 weeks, by which time the conjunctival injection had disappeared and the corneal haze had partially cleared. The endothelium seemed intact, and there was an occasional free cell in the anterior chamber. Refraction with a plus 13 sphere and a plus 50 cylinder axis 180 gave 6/60 vision. The eye being quiet, it was considered wise to stop treatment. Now 6/60 in itself is not remarkable vision, but in contrast to a lost eye which I think we might have had without the use of Pregl's solution, it is extremely desirable.

Case 2: W. B., 8 years of age, entered the hospital on October 9 with a history of having been struck in the right eye the day previous with a pair of scissors. Examination showed the cornea slightly hazy with a horizontal laceration extending almost the width of the cornea about 4 mm. below the inferior pupillary border. The iris had a muddy appearance throughout, and there was a semblance of exudate at the inferior angle which was incarcerated in the corneal wound. It did not react to light. The lens was cataractous with lens material protruding through a puncture wound in the anterior lens capsule. The anterior chamber had been evacuated. On the day after admission the patient was taken to the operating room, where the iris was freed from the cornea by iridectomy, part of the anterior capsule being removed and much of the lens material being washed out by irrigation. At the termination of the operative procedure 10 minims of Pregl's solution was injected directly into the anterior chamber, after which the usual dressings were applied, and the patient returned to his room. On dressing the eye the following day the cornea was still hazy, the wound was closed, and the anterior chamber was shallow but forming. Two days later the anterior chamber was formed, and the cornea was clear. There still remained a large amount of cortical material in the former pupillary space. The case was discharged on November 5 with the eye quiet. While in the hospital the patient received additional therapy of atropine, salicylates with soda, and mercury rubs. He has been seen 4 times since his discharge. Vision on November 9 was 2/60 in the eye operated on, and there was a slight photophobia present. This photophobia had disappeared at the time of the last visit to the clinic. The eye was then quiet, and the patient had made a good recovery.

These 2 cases were presented not so much because of the severity of the infection treated, but because of the 2 different methods of administering the Pregl's solution. In the first case it was given subconjunctivally; in the second it was injected directly into the anterior chamber.

In brief, Pregl's iodine solution appears to be a valuable therapeutic agent in infections of the anterior segment of the eye, especially when there is danger of the formation of corneal opacities.

Gastric Leiomyoma.—The number of gastric leiomyomas reported in the literature are still comparatively few. Our chief interest in this condition is the fact that it has been diagnosed in our hospital as carcinoma of the stomach, and because of that fact at least one patient was almost deprived of the benefit of operation. Even though the clinician considers the diagnosis of benign tumor when confronted with such a lesion, critical examination of all the evidence may not permit him to make such a diagnosis. . . .

The diagnosis is seldom made clinically, although certain features in roentgen examination are suggestive. Diagnosis without roentgen examination is impossible. There are frequently an absent or low free HCl, anemia and persistent blood in the stool, which, with the finding of a filling defect by roentgen examination, usually lead one to think of carcinoma. No mass can be palpated as a rule. Moore, reviewing the roentgenologic signs suggestive of benign gastric tumors, concludes that the filling defect is circumscribed and without associated spasm or deformity of the stomach. There is no interference with peristalsis and no distortion of the rugae. . . .

Summary.—1. A benign tumor of the stomach may be diagnosed malignant after careful clinical roentgen and gross examination of the patient, or even following study of the frozen section.

2. The frequency of benign tumors and of infective granulomas of the stomach and the fact that they are usually diagnosed as gastric carcinomas make it imperative that pathologic proof of the true condition of such tumors should be required before the diagnosis of gastric carcinoma is accepted for statistical purposes.

3. The majority of patients with suspected malignant tumors of the stomach should have the benefit of exploratory operation and biopsy, even though the tumor is considered inoperable.

4. Gastric leiomyomas which are apparently benign occasionally metastasize.

Extract from article by John L. Lindquist, M.D., and Harry E. Mock, M.D., Chicago, Ill., *Northwest Medicine, February*, 1937, p. 42.

INFECTIOUS DIARRHEAS IN CHILDREN[*]

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The Children's Hospital with its 200 beds offers one of the best opportunities for the study of infant diarrheas, not only because of its large inpatient facilities but also because of its cosmopolitan clientele. It serves not only the District of Columbia but also neighboring Virginia and Maryland. The statistics of the hospital show that since 1933 to the present date there have been 750 cases of diarrhea. These may be divided into 556 cases of simple non-infectious diarrhea, either alone or complicating some other disease, and 194 cases of true infectious etiology. Only the latter group need concern us here.

The diagnosis of a specific infectious diarrhea is one which entails great difficulty, since only in a few types of bacillary dysentery are there present true clinical syndromes. In our laboratory, the clinical diagnosis of dysentery (infectious) as based on bloody mucoid stools, history and response to treatment, is corroborated by bacteriological study of the stools. In numerous cases it has been the experience of the bacteriologist to fail in isolation of specific causative organisms from stools during life, but to be successful with material scrapped from the gastro-intestinal tract at necropsy.

Within the past 3 years attempts have been made by the laboratory staff to perfect the diagnostic technic. At the present time it is the custom to obtain 3 samples of stools, taken the same day with a sterile catheter, which are inoculated onto a brain-heart infusion broth for half an hour at 37°C. A suspension of this mixture is then transferred to eosin-methylene blue and blood agar plates and incubated for 24 hours. At this time the plates are examined for typical colony formation and fermentation by the streptococci, staphylococci, and organisms of the typhoid-dysentery group. Suspected colonies of the latter type are transferred to Russell's double sugar (stab method) and incubated for another 24 hours. Acid tubes are discarded. Alkaline slants with acid butts indicate a member of the typhoid-dysentery group; gas formation is indicative of the typhoid bacillus. Representative suspected colonies are then transferred to maltose, dextrose, lactose, mannite, and saccharose broth, incubated for 24 hours and examined for gas and acid formation. The final diagnosis is based on indole fermentation and the microscopic demonstration of motility.

TABLE 1

INFECTING ORGANISMS

CAUSATIVE AGENT	1933	1934	1935	1936
Eberthella paradysenteriae Flexner	8	5	8	4
Eberthella paradysenteriae Hiss	28	7	5	16
Eberthella paradysenteriae Shiga		1		
Eberthella typhi	16	4	14	5
Salmonella paradysenteriae A			1	2
Salmonella paradysenteriae B	1		3	3
Streptococci	5	9	3	35
Salmonella enteritidis Gaertner	1	1		1
Lactobacillus bulgaricus	1			
Eberthella belfastiensis			1	
Salmonella morgani			2	5
Escherichia coli				1
Eberthella pyogenes				1

Table 1 gives a bacteriological summary of the causative agents as found in this survey of the cases of infectious diarrheas since 1933. It is interesting to note that whereas in the District of Columbia the greatest number of cases are due to Eberthella paradysenteriae Hiss, workers in Maryland (Wilkins), West Virginia (Lyon), and New York (Wollstein) find that from 25 to 80 per cent of their cases are due to Eberthella paradysenteriae Flexner.

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[*] From the Children's Hospital. Reported by courtesy of Frank Leech, M.D., Chairman, Medical Staff.

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The reports found in the literature relating to the bacteriology of the stools from infants with diarrhea show great variation as to those in which the dysentery bacillus was found. The lack of uniformity seemed to depend on (1) the technic used in procuring material for culture, (2) the type of patient under observation, (3) seasonal variation in incidence of dysentery infection, and (4) geographical and environmental locality.

Talbot says that the condition is most frequently seen in the hot summer months, particularly July and August. In our series the peak of incidence for the 4 years falls between July and October, with a mean peak for this period occurring in September.

The fact that there is no characteristic lesion found in the gastro-intestinal tract of the majority of infants succumbing to this condition indicates that factors other than gastro-intestinal damage must be operative, at least in those cases in which such specific disease as dysentery can be excluded.

Most writers pay little attention to the age incidence and susceptibility other than to state that infants and children are particularly prone to present this clinical syndrome. In our opinion the question of age distribution is of prime importance if one is to seek adequate measures to combat this scourge of infancy. Table 2 gives the age distribution and racial distribution of the infectious diarrheas at Children's Hospital for the past 4 years.

It brings out the very important point of the higher incidence in colored children, due mainly to their socio-economic status and accompanying ignorance. A close inspection readily reveals the prime factors which are the causative or rather catalytic factors in the development of dysentery. In the District of Columbia the sanitary and hygienic surroundings of the colored people, overcrowding, proximity with improperly disposed sewage, lack of proper individual hygienic care and prolonged warm humid atmospheres with heavy infestation by flies, are of such nature as to be conducive to the development and spread of the disease. With the white infants, on the other hand, we have a similar problem of socio-economic status. The majority of the white patients came from the small hamlets and towns of nearby Virginia and Maryland where there might not be proper sewage disposal, etc. The problem apparently hinges largely on the socio-economic status of the patient's parents.

Again, reference to this same table reveals that the highest incidence occurs between the ages of 6 to 12 months. It is at this period in life that the baby is first weaned and comes in contact with food of a nature not prepared especially for him. It is during this time that most of the non-infectious diarrheas are apt to occur since it takes some time for the gastro-intestinal tract of the infant to accustom itself to a new type of diet. It is a well-known fact that rarely does dysentery develop in exclusively breast-fed infants. At the Thomas Wilson Sanitarium Welfare Clinics at Baltimore a survey was undertaken to determine the incidence of dysentery and simple diarrheas. The results are worth noting. The incidence of dysentery was between 7.6 and 12.9 per cent. Approximately a

TABLE 2

Age Incidence and Race

AGE GROUPS	WHITE	COLORED
1933		
0 to 6 months	3	3
6 to 12 months	7	10
12 to 24 months	5	9
24 months up (16 cases of typhoid)	10	14
1934		
0 to 6 months	2	1
6 to 12 months	3	6
12 to 24 months	1	4
24 months up (4 cases of typhoid)	5	5
1935		
0 to 6 months	1	1
6 to 12 months	2	5
12 to 24 months	2	2
24 months up (5 cases of typhoid)	9	12
1936		
0 to 6 months	8	6
6 to 12 months	8	13
12 to 24 months (2 cases of typhoid)	7	11
24 months up (3 cases of typhoid)	7	11

fourth of the infants at this institution were exclusively breast fed. Among these only 10 per cent developed simple diarrheas and none developed dysentery. Among the artificially fed group only 50 per cent remained well; 33 per cent developed simple diarrheas, and 17 per cent had typical dysentery. The figures obtained at our hospital closely parallel those obtained in Baltimore.

Summary

1. Since 1933 the Children's Hospital has had 750 cases of dysentery, of which 194 were of true infectious origin.
2. The mean height incidence of the 4 years occurred in September.
3. Of the 194 cases of infectious diarrhea, the greater majority were negroes.
4. Artificial feeding and the socio-economic status of the family are important factors in the development of diarrhea.

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Recurrent Functional Hypoglycemia in Juveniles. A Review with Particular Reference to its Convulsive Manifestations.—Since the genesis of simple methods for the determination of blood sugar, there have been many publications regarding the conditions in which hypoglycemia occurs. Most of these have been concerned with the hypoglycemia of adults, especially with that condition known as hyperinsulinism. However, there have been relatively few communications on the occurrence of hypoglycemia in children, and not a great deal of stress has been laid upon convulsions as an outstanding symptom of their defective sugar metabolism.

The association of convulsions with hypoglycemia was first pointed out by Josephs in 1924. He described the case of a child with recurrent vomiting attacks, accompanied by convulsive seizures, in whom the blood sugar on such an occasion was found to be 37 mgm. A search of the literature for the past 12 years reveals that there have been reported 35 cases of convulsions in juveniles in whom hypoglycemia was, presumably, the sole etiological factor of importance. It is of significance to note that among this group, the hypoglycemia which prevailed was apparently functional or spontaneous in 32 cases. Only 3 showed demonstrable organic lesions; 1 a case of multiple pancreatic adenomata with hyperinsuiinism reported by Wolf, another, a case of islet cell hyperplasia discussed by Dannenberg, and the third, an example of hepatic insufficiency incident to profound fatty degeneration, reported by Kramer. In addition, 1 of the cases reported by Higgons occurred in a newly born infant whose mother was a diabetic. The child recovered, hence this was probably a case of transient hypertrophy of the Islands of Langerhans.

At the Infants' and Children's Hospital, Boston, we have had an opportunity to observe 10 cases of functional hypoglycemia of the recurrent type associated with convulsions. In 7 of these, hypoglycemia was the only finding of significance. Two cases showed evidence of cortical atrophy that probably was contributory, although it might have been the result of the convulsions; and a third had cerebral edema which was thought to be secondary to a fulminating infection. . . .

Incidence.—Spontaneous hypoglycemia of the recurrent type associated with convulsions may have its onset at any period throughout infancy and childhood, although the majority of cases are seen in the age group from 1 to 3 years. It is relatively infrequent under 1 year of age, and it is not common for the first attack to appear after the age of 3.

Although our series is too small to render sex of any great importance, attention is called to the fact that 8 of the 11 cases occurred in males. An analysis of the cases reported in the literature also shows a preponderance of males over females, with a ratio of 2 to 1. . . .

Diagnosis.—The diagnosis of convulsions associated with hypoglycemia may be suspected in those children in whom the attacks occur late at night, in the early morning, or several hours postprandially, with a preceding history of anorexia, fever, vomiting, excessive exercise, or excitement. There is nothing diagnostic about the character of the convulsions, and physical examination shows very little of significance, except for evidence of ketosis. A diminution of the spinal fluid sugar in an otherwise normal spinal fluid is a highly suggestive finding of great diagnostic value. For most practical purposes, spinal fluid sugar, in the absence of red cells, may be assumed to be one half of the blood sugar. This low spinal fluid sugar value served as a diagnostic lead in several of our cases.

Final diagnosis rests upon the finding of a convulsive or post-convulsive blood sugar of less than 70 mgm. It should be stressed that glycemia readings obtained at other times are practically valueless. Spontaneous hypoglycemia of this type is intermittent, and between attacks, essentially normal sugar levels exist.

A dextrose tolerance test at the time of convulsions is impractical, and between attacks it is not of great diagnostic assistance, although there is some slight tendency toward an increased tolerance to carbohydrate in these cases. A combined analysis of the curves in this series, plus those reported in the literature on juvenile cases, shows an average maximal blood sugar rise of 48 mgm. The average "normal" maximal rise for children of this age is quoted as approximately 67 mgm. Rather frequently, these cases also exhibit a tendency toward the approach of hypoglycemic levels at the end of 3 to 4 hours. Of suggestive importance is the finding of Dannenberg in his case, that the use of excessively large amounts of dextrose (4 grams per kilogram of body weight) in the test meal, showed a marked increase in the dextrose tolerance, with a definitely hypoglycemic end value to the curve. Since his case was one of hypertrophy of the islet cells, this finding may more properly be indicative of a true hyperinsulinism, in contrast to functional hypoglycemia. However, the variation among normal children is so great, and the cases of our series demonstrated such individual variations, that one is hardly justified in considering them conclusive. Likewise, the response to epinephrine was somewhat less than is usually found, the average rise (maximal) in our series being 33 mgm. There was no correlation between the dextrose tolerance and adrenalin response.

It is obvious that other convulsive disorders in childhood, such as tetany, meningismus, organic involvement of the central nervous system, including lead encephalopathy, must be excluded by the appropriate diagnostic measures.

Treatment.—The therapeutic procedure of choice during an attack is the immediate administration of dextrose by phleboclysis. For this purpose, a solution of 10 per cent strength, in quantities calculated at 10 cc. per pound of body weight, has been found to be most effective. The total amount should not exceed 300 cc., and administration must be done slowly to prevent diuresis, and subsequent loss of dextrose through the kidneys. This procedure may well be complemented with saline hypodermoclysis to combat any existing dehydration. Results are usually dramatic, with the prompt cessation of convulsions, and rapid recovery. Occasionally drowsiness persists for several hours. Should difficulties be encountered with the intravenous technic, a 3 to 5 per cent solution of dextrose by hypodermoclysis is useful.

Prophylactic treatment is largely dietary. Attacks are prevented in most cases by the use of a diet moderately high in carbohydrates, augmented by a mid-morning, a mid-afternoon, and after-supper feeding. Such a regimen usually controls hypoglycemia of this type. There is a remote possibility that such a high carbohydrate intake would stimulate the islet cells, with an overproduction of insulin. Several adult cases have had their attacks aggravated by a high carbohydrate diet, but some of these were subsequently found to have tumors of the pancreas. . . .

The possibility of pancreatic neoplasm in children, even though remote, should be kept in mind. If the course is progressive, and unaccompanied by demonstrable dietary benefit, exploratory laparotomy should be considered.

In cases of suspected hyperinsulinism without evidence of tumor, subtotal pancreatectomy has been performed, without clinical improvement in most cases. This procedure does not seem justified in childhood.

Particular attention should be directed toward carbohydrate feedings at the onset of infections, as attacks are especially prone to occur at this time. Should the necessity for any surgical procedure arise in these hypoglycemic children, it is essential that their preoperative care should embrace the liberal use of dextrose solutions. . . .

Extract from article by Robert E. Jennings, M.D., East Orange, N.J., and John Mott Rector, M.D., San Francisco, Calif., *Journal, Medical Society of New Jersey, February*, 1937, p. 79.

COURT OF APPEALS DECISIONS*

WITH EXCERPTS OF THE EVIDENCE IN CASES BROUGHT BY AND AGAINST WASHINGTON PHYSICIANS

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It is believed that the members of this Society will be interested in a brief review of cases involving medicine and surgery which have been decided by the United States Court of Appeals of the District of Columbia. These cases, at the time of trial in the lower court, and later on hearing in the appellate tribunal, were of more or less importance to medical men practicing in this jurisdiction. They involved numerous questions of the correctness of diagnosis and treatment, the administration of anesthetics, the obtaining of a patient's consent to an operation, the reasonableness of professional charges, and the right to practice and what constitutes the practice of medicine.

When decisions were rendered by the Court of Appeals the interest which theretofore had been local was widened in scope, since the opinions then became part of the literature of the law. Very soon thereafter, it became noticeable that these decisions were being cited with approval by courts in other jurisdictions. Two cases which stand out conspicuously by reason of the frequency with which they have been cited with approval are *Sweeney v. Erving* (35 App. D.C. 57) and *Levy v. Vaughan* (42 App. D.C. 146).

Sweeney v. Erving, supra, was one of the first decisions of an appellate tribunal on the subject of X-ray diagnosis. In that case the plaintiff had been sent by Dr. James Kerr, a surgeon, to Dr. William G. Erving for an X-ray diagnosis, the plaintiff claiming that she had been injured in a railroad accident. An X-ray burn followed the fourth exposure. Plaintiff contended that X-ray diagnosis was not on the same plane as diagnosis made in the usual manner by a physician or surgeon but was more in the nature of a mechanical act. At the time this case was tried (1909) decisions in X-ray cases were relatively few in number and were not uniform. One view which had some following was that the mere fact that a plaintiff sustained an X-ray burn was of itself evidence of improper treatment. The Court of Appeals settled this question in the District of Columbia in a decision which was affirmed by the Supreme Court of the United States and which has been very frequently quoted and relied upon. The Court of Appeals said:

> "The evidence in this record justifies the finding that the use of the X-ray in the diagnosis and treatment of human ills is recognized and practiced by the medical profession. Such being the case, we see no reason why a different rule should apply to practitioners in this line than is applied to other practitioners."

Levy v. Vaughan, supra, determined the question, in this jurisdiction, as to the liability of an operating surgeon for the administration of an anesthetic. Moreover, it is probable that no decision of the courts of the District of Columbia has been referred to more often, and with approval, by courts in other jurisdictions. The defendant, Dr. George Tully Vaughan, had been engaged to perform an operation on one Beckett for hernia. Dr. Vaughan made an examination of the heart and lungs of the patient, and a similar examination was made by the anesthetist. Great stress was laid on the fact that the anesthetist was a medical student in his last year of a 4-year course. It was in evidence that he studied the subject of administering ether and observed its administration in at least 1,000 cases and had actually administered ether before in 8 or 10 cases. Two graduate physicians were in and out of the room during the administration. A moderate amount of ether was administered during 25 or 30 minutes, and no unusual condition was noticed until the patient had been placed on the operating table. It was then observed that he was blue in the face, i.e., cyanotic. Dr. Vaughan, who was then present in the operating room, noticed the condition and at once started artificial respiration and directed that the patient be taken back to the ward. It the ward, remedies were used and Dr. Vaughan again performed artificial respiration, but the patient's respiration ceased and he died. An autopsy the patient's heart was found to be in a state of fatty degeneration.

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* Read before the Society, December 16, 1936.

On the trial of the case before Chief Justice Clabaugh of the Supreme Court of the District of Columbia, Dr. J. Wesley Bovée testified that it was the custom in the Mayo Clinic in Rochester, Minnesota, to entrust the administration of ether to advanced medical students of experience, and also it was in evidence that a similar custom prevailed in the District of Columbia. It was brought out that the 2 graduate physicians who were present during the administration of the ether were not licensed to practice in the District of Columbia, but the court held that there was nothing to warrant an inference that the possession of a District license would have added to their competency. Dr. Wilfred M. Barton, a physician and teacher of medicine of long experience, testified that the administration of an anesthetic is not technically difficult and that students are permitted to do it.

As to the condition of the patient's heart and lungs, it was in evidence that Dr. Vaughan had twice examined him, this in addition to the examinations made by the anesthetist. When a question was propounded to Dr. Vaughan undertaking to pin him down as to the length of time occupied by such an examination, he answered that it was a sufficient length of time to establish the fact in his own mind. All the physicians who testified stated that it was practically impossible to diagnose fatty degeneration of the heart in advance of an autopsy, and that there was no other affection of any kind so far as the patient's heart was concerned.

The trial justice permitted the defendant to introduce his evidence and then in a lengthy dissertation to the jury, in which he summed up all the evidence, he directed the jury to return a verdict for the defendant.

On appeal, Chief Justice Shepard of the Court of Appeals of the District of Columbia commented at considerable length on the evidence which sought to impute liability on the defendant. He sustained none of the exceptions taken by the plaintiff and affirmed all the rulings made by the trial judge. The charge to the jury made by Chief Justice Clabaugh, which was in reality an opinion, was commented upon for its fairness and for the manner in which it fully analyzed the questions raised in the case and the unusual method was adopted of including the opinion of the lower court in the bound volume of the Court of Appeals decisions.

The latter case was referred to by the Court of Appeals in its decision in the case of *Cayton v. English* (57 App. D.C. 324), which was an action for malpractice brought by Rosa Cayton against Dr. Merton A. English who was described in the declaration as representing himself "to be a practitioner especially skilled in the practice of osteopathy." It may be here remarked that Dr. English in his testimony stated that he was duly registered and qualified to practice both medicine and osteopathy in the District of Columbia. Plaintiff alleged that she employed the defendant to treat her for relief from headaches and high blood pressure and that in an unskilled, careless, and negligent manner, in manipulating and adjusting her body and limbs he caused a large mass to bulge forward about 1 inch below the great trochanter of plaintiff's left leg and caused a diagonal rupture of the fascia lata in consequence of which she suffered great pain and was compelled to undergo a surgical operation for relief.

Plaintiff called a large number of physicians as witnesses. Dr. Samuel L. Owens testified that he had been called on the day that the patient had received treatment at the office of Dr. English, and had treated her for a condition that he thought was sciatica and could not recall seeing any protrusion or swelling.

Dr. Harry S. Lewis, who saw the patient more than a year after the treatment by Dr. English, was of the opinion that forceful manipulation, if sufficiently violent, might have resulted in a rupture of the fascia lata.

Dr. Harry W. Miller, a surgeon and chief of staff of the Washington Sanitarium and Hospital, testified that the patient was admitted to that institution the month following the treatment by Dr. English. He was asked as to whether he had formed an opinion as to how the injury could have occurred, to which he responded that the patient's condition must have been due to some injury but that he did not know how a physician could decide how an injury occurred. Dr. Daniel H. Kress, connected with the same institution, testified that he was unable to tell whether the condition found was the result of any treatment the patient had. And still another member of the staff of the Washington Sanitarium and Hospital, Dr. Geoffrey Williams, testified that he "had never seen a rupture of the fascia lata similar to this one."

Dr. Joseph A. Jeffries testified that he had seen the plaintiff about the time of the alleged injury and recommended that she see a surgeon and further that he was not familiar with osteopathic treatment and knew nothing about it.

The only osteopath called by the plaintiff was Dr. Norman C. Glover, who testified "that he could not see how an injury could ever follow an adduction or treatment."

Dr. English, testifying in his own behalf, said that the patient had been recommended to him by a Major Poston, a naturopath, and that he had made a written report of the case to Major Poston. Dr. English stated that before treating her he had noticed that she limped.

The jury found in favor of the defendant, and plaintiff appealed to the Court of Appeals. The opinion of the Court of Appeals, written by Mr. Justice Robb, quoted from what is probably the leading case in the United States on malpractice, *Ewing v. Goode* (78 Fed. 442), an opinion written by Judge Taft, later President of the United States, and later Chief Justice of the United States. In that opinion Judge Taft said:

> "Before the plaintiff can recover, she must show by affirmative evidence—first, that defendant was unskilled or negligent; and second, that this want of skill or care caused injury to the plaintiff. If either element is lacking in her proof, she has presented no case for the consideration of the jury. The naked facts that defendant performed operations upon her eye and that pain followed and that subsequently the eye was in such a bad condition that it had to be extracted establish neither the negligence and unskilfulness of the treatment nor the causal connection between it and the unfortunate event."

Hazen v. Mullen (59 App. D.C. 3) is another case decided by the Court of Appeals in favor of a physician, the decision being based upon Judge Taft's opinion in *Ewing v. Goode, supra.* It was alleged that in giving X-ray treatment for tuberculous adenitis, Dr. Henry H. Hazen did not properly use the apparatus, as a result of which the patient was permanently disfigured, scarred and maimed. On the first trial the jury gave plaintiff a verdict for $20,000.00 which the Court set aside. On a retrial, the verdict for plaintiff was for $15,000.00. It is evident that the weight of medical evidence made no impression on the jury, for as against Dr. William B. Carr, the only physician testifying for plaintiff, the defense put on the stand Drs. Thomas A. Groover, F. J. Eichenlaub, Arthur C. Christie, Truman Abbe and Roy D. Adams. The lower court permitted the verdict to stand, but this was reversed by the appellate tribunal.

Burroughs v. Crichton (48 App. D.C. 596) involved the question of whether the consent of the husband is necessary for the performance of an operation on his wife, the wife having given her consent.

James E. Burroughs brought suit against Dr. MacPherson Crichton alleging that the defendant, by false representations, had obtained plaintiff's consent to an operation on plaintiff's wife and further that after the operation, although the defendant had contracted to attend the patient, he failed to do so and that it was necessary to call another physician. The plaintiff alleged that defendant knew that plaintiff's wife was afflicted with cancer, but informed the plaintiff that she "was affected with an ordinary benign tumor," that defendant operated, that the patient remained in the hospital for a month and a half and then returned home in a dangerous condition and suffered pain until her death a few months thereafter. Defendant demurred on the ground that, admitting the facts alleged in the amended declaration to be true, they did not state a cause of action. The Court sustained the demurrer and plaintiff took the case to the Court of Appeals. The Court of Appeals held that the declaration was fatally defective in that it contained no averment that the plaintiff herself did not consent to the operation. The court remarked that the theory that the husband exercises the same control over his wife as is exercised by the owner of a chattel was untenable, using this language:

> "A wife, in the full possession of her faculties, is as much entitled, both morally and legally, to determine whether she shall submit herself to an operation as is the husband in respect to an operation on himself. And where a wife, in such circumstances, consents to an operation which is skilfully performed, the surgeon is not liable to the husband in damages."

The Court of Appeals quoted at considerable length from the case of *Janney v. Housekeeper* (70 Md. 162), in which the court said:

> "The husband had no power to withhold from his wife the medical assistance which her case might require. . . . The consent of the wife, and not that of the husband, was necessary."

As to the second count in the declaration, however, which was based on the failure of the plaintiff to give postoperative attention, the Court of Appeals reversed the lower court. It was alleged that defendant, for the sum of $200.00 had agreed not only to perform the operation but to give necessary professional attendance, care and treatment after the operation, both at the hospital and at her home; and that although the plaintiff had performed his part of the contract, defendant neglected to attend the patient; and, because of her intense suffering, it was necessary to call another physician at additional expense. The Court of Appeals held that this averment, if true, constituted a cause of action and reversed the judgment in part, returning the case to the lower court for further proceedings.

Dr. Joseph J. Kaveney brought suit against the American Security and Trust Company as executor of the estate of John E. Herrell (*American Security and Trust Co. v. Kaveney*, 39 App. D.C. 223) for $37,680.00. This probably was the largest medical bill ever brought to the attention of the local courts. The amount was set out in an itemized account under the head of "extraordinary medical and surgical services." These services extended from September 2, 1906, to March 30, 1909, the date of Mr. Herrell's death. One item was for 16 days' attendance in Virginia at $100.00 per day, and the remaining items were for catheterizing and irrigating the bladder from 3 to 5 or more times a day at a charge of $10.00 an operation.

Because of the prohibition of Sections 1064 and 1073 of the Code against the surviving party testifying as to transactions with a deceased party, and against physicians disclosing information acquired in attending a patient, Dr. Kaveney was not permitted to testify as to conversations with or treatment given the patient. He did, however, testify as to his medical training, that he was a licensed physician, told of the number of times that he had seen Mr. Herrell, that for most of the period covered by the claim he had lived at Mr. Herrell's house, that in his hospital and private practice he had seen between 50 and 100 prostatic cases, and that while a hospital steward on duty at the Naval Hospital it had been his duty to catheterize patients.

From the evidence of several lay witnesses it appeared that at the time of death Mr. Herrell was 80 years of age, a man of considerable means, president of a local bank, that he had frequently stated that he suffered from a serious enlargement of the prostate gland and that under no conditions would he submit to an operation because he feared it would result fatally; and that he often had declared that Dr. Kaveney catheterized him from 3 to 5 times daily, and had praised the skill and efficiency of the doctor and attributed the saving of his life to the doctor's attendance upon him in Virginia in 1906.

Having neither wife nor children, Mr. Herrell employed a cousin, Miss Herrell, as his housekeeper, and during the period covered by this claim Dr. Kaveney married Miss Herrell and thereafter occupied a room at Mr. Herrell's house. Mr. Herrell refused to permit Dr. Kaveney to have a telephone in the house for fear he might be called out at night by other persons. There was no evidence of actual services rendered by Dr. Kaveney except for a short period prior to September 2, 1906, and from February 22, 1909, to the date of Mr. Herrell's death the following month, during which time he had a male nurse.

It is interesting to observe the variance in the testimony of the medical witnesses as to the value of the services rendered by Dr. Kaveney. There was rather wide divergence in the opinions which they expressed in response to a uniform hypothetical question covering these services.

Drs. H. J. Crosson, John R. Wellington, Frank Leech, Richard Kingsman, James F. Mitchell and John Thomas Kelley, Jr., all approved the charge of $10.00 for each catheterization and $100.00 a day while attending the patient in Virginia. Dr. Kingsman was interrogated at length as to whether he had taken into account the fact that Dr. Kaveney was a beginner in medical practice. Dr. Kingsman replied that this was immaterial and that the proper standard upon which to base judgment was whether the doctor rendered the necessary service and relieved the patient, in which event his services were worth as much as any other physician.

Dr. George Tully Vaughan, who was the last medical witness for the plaintiff, had been called twice in consultation with Dr. Kaveney. Of course, this witness also was under the prohibition against disclosing confidential information. From questions asked by defendant's counsel, it is clear they took the position that attendance over so long a period could have been avoided by a surgical operation. On cross-examination Dr. Vaughan was asked whether, in a hypothetical case which was so serious as to require an operation, a physician should continue treatment without the operation and perform the act of drawing the water 6 or 8 times a day. The advice that Dr. Vaughan had given Mr. Herrell can readily be surmised from his reply, which was "if the patient was so pig-headed as to refuse relief that might be permanent" there was no reason why a physician should not give such relief as the patient would allow.

Drs. Harry A. Fowler, J. Wesley Bovée, Sterling Ruffin, L. L. Friedrich, Charles R. Luce, J. W. Hodges, G. C. Clark, J. Ramsay Nevitt, John H. Metzerott, and E. T. M. Franklin testified that in the light of all the circumstances in this case they considered Dr. Kaveney's bill to be excessive.

Dr. J. B. Gregg Custis, who had been the patient's physician for many years and practically to the time of the calling of Dr. Kaveney, testified that while he knew the general charges for services such as described, he could not state what would be a fair and reasonable charge in this case.

The verdict of the jury was in Dr. Kaveneys favor in the amount of $27,476.00. Immediately the defendant moved for a new trial, the principal grounds for the motion being that the amount was grossly excessive and was arrived at in an irregular and illegal manner. As to the latter, an affidavit was filed setting forth that this was a "quotient" verdict effected by each juryman writing an amount, the amounts then being added and the total divided by 12. Three jurors joined in another affidavit from which it appeared that it had not been decided in advance to accept the quotient and that the decision was reached after the amount had been determined. In denying the motion for new trial, the presiding judge commented at length upon the fact that it had been argued that $27,476.00 was altogether an unreasonable allowance for a young doctor and that it had been claimed that he could not possibly have earned that amount. The Court, however, took another view, expressing it in these words:

> "He was a young man who had just begun to practice medicine. It was said that he could not possibly have earned that amount.
>
> "That is one view that might be taken of it. Another view is that he was beginning the practice of medicine with the expectation of making it his calling for life, and that 2 years and 7 months were taken out of that life as a whole, as a unit.
>
> "Supposing a musician, violinist, wishes to become famous in his art, and is just beginning his career. If he succeeds, he will be able to earn a very great income and make a great name for himself. But one of his neighbors likes to hear him play 'Yankee Doodle,' and so he engages him to play that tune constantly for 3 years, and no other tune."

In arguing the case before the Court of Appeals, counsel for the defendant contended that inasmuch as there was no evidence as to actual rendering of services except for the 16 days when the patient was in Virginia and during the month preceding death, the claim should be confined to these periods thus fixing the limit of recovery at $3,730.00. With this contention the Court of Appeals did not agree, remarking that "it can hardly be supposed that such services were performed in the presence of witnesses." The judgment of the lower court was affirmed.

Nathan A. Springer, who claimed to be a physician but who was not licensed to practice in the District of Columbia, was the President and General Manager of a sanitarium located between Baltimore and Washington on the Baltimore and Ohio Railroad. Springer claimed to be the discoverer of a system of treatment for drunkenness and drug habits and to operate about 20 institutions in different states. A yellow paper circular had been distributed in the District of Columbia advertising the Springer Sanitarium and giving the Washington address of the sanitarium as a drug store at Fifth and G Streets, N.W. On the circular appeared the name "N. A. Springer, M.D., President and General Manager." Dr. Springer was charged in the Police Court with practicing medicine without having first obtained a license so to do in the manner required by law.

It appeared from Dr. Springer's testimony that he never administered the treatment but always employed a local physician to do so and that he, Springer, confined himself to managing the business. His testimony further was to the effect that he explained the drugs to be used to the local physicians who were to treat his patients and he left it to the local physicians when and in what quantities to administer the drugs. He claimed that he did not diagnose any cases, prescribe for the patients or administer the medicine, although he admitted that the local physicians administered the medicines which he provided.

The prosecution put on the stand 2 local physicians. One of these, Dr. Frederick O. Roman, testified that Springer had called at his office, saying that he understood Dr. Roman had patients needing treatment for acute alcoholism and he asked if they would take the Springer treatment. Dr. Roman testified that the patients declined to do so and he did not submit them to the Springer treatment.

Dr. John R. Atwell, a registered physician, testified that Springer had engaged him to see 4 patients in the District of Columbia. That 1 of these resided at the Shoreham Hotel and that he, Dr. Atwell, visited him 3 or 4 times a week, sometimes twice a day at his own discretion, and visited the other patients under the same circumstances. He stated that he treated these patients with Springer's medicines which Springer had left at the places at which the patients were staying, that he used his own discretion as to frequency of doses, and whenever complications arose he used his own judgment. Dr. Atwell testified that he had been employed at a regular price per visit.

In charging the jury, the Court made it clear that there could be no subterfuge or indirect method adopted to circumvent the law, using this language, "Gentlemen of the Jury, the law looks with great disfavor upon dissimulation. A man cannot do indirectly what he cannot do directly. That which is forbidden by the law he should not do indirectly if he cannot do it directly."

The defendant was convicted in the Police Court and the case went to the Court of Appeals on a writ of error (*Springer v. District of Columbia*, 23 App. D.C. 59). In affirming the action of the Police Court, the Court of Appeals said that while neither the circular nor the fact that the defendant had registered at a Washington Hotel as "Dr. N. A. Springer" separately or together would be sufficient proof of a violation of a statute they were nevertheless circumstances tending to show, in connection with the other evidence, that the defendant held himself out as a practitioner in the District of Columbia. Although the statute does not declare what specific acts shall constitute "practicing medicine" or what it is to "publicly profess to do so," the courts will determine whether the facts proved in a particular case bring it within the terms of the statute, taking these facts in the sense in which they are commonly understood.

Further, the Court said, "Selling his compounds to such persons as he might examine and and pronounce fit subjects of medical treatment was 'practicing medicine' as much as if he had given them, instead, an ordinary prescription that could be satisfied in any regular drug store."

The court experienced no difficulty in determining that Springer was practicing medicine when he "obtained patients, diagnosed their cases, decided that they were suffering from a malady for which he had discovered or compounded a remedy, prescribed and furnished that remedy and employed other physicians to take immediate charge of the patients and administer the same."

Dr. Lewis B. Thomson had been refused a license to practice medicine in the District of Columbia, whereupon he made application to the Supreme Court of the District of Columbia for a writ of mandamus to compel the Board of Medical Supervisors to grant the license (*Thomson v. Custis*, 35 App. D.C. 247).

The Board, answering a rule to show cause, submitted that Dr. Thomson had asked for a license by reciprocity on a showing that he had been licensed in the State of Maryland and had practiced (in Maryland) for more than 2 years prior to the date of making his application in the District of Columbia, but that the conditions under which he had passed his examination in Maryland were not equivalent to conditions existing in the District of Columbia. The Board of Medical Examiners set forth certain rules which it had adopted regulating the examination of candidates and insisted that under the rules in force in the District of Columbia Dr. Thomson could not have obtained a license. In other words, the contention of the Board was that the requirements in the State of Maryland were not equivalent to those in the District of Columbia; to all of which Dr. Thomson responded that the examination in Maryland "was fundamental in character and tested his fitness to practice medicine and surgery."

The Supreme Court of the District of Columbia refused a writ of mandamus and an appeal was taken to the Court of Appeals. In the opinion of that court, the rules made by the Board of Medical Examiners were not regarded with any particular sanctity. The Court said:

> "The Board claims the power, by rules and regulations, to determine what shall constitute 'conditions equivalent' under the statute before reciprocal relations between Maryland and this District can be said to exist. We think equivalent conditions exist under this statute by virtue of the provisions of law and not under the rules of the Board. . . . The Maryland Board may have an entirely different set of rules for carrying into effect substantially the same statute as ours; but that is a mere matter of local procedure which cannot affect the reciprocal rights of practitioners of one jurisdiction to practice in another, provided they meet the requirements of the Board in the State where originally admitted and the provisions of the statute in the jurisdiction where they desire to practice. If the contention of the Board be correct, it lies within its power to prescribe conditions of admission to the Boards of all States and Territories in order to entitle any of their licentiates to practice in this District, thereby absolutely annulling the express provisions of this statute. It is against public policy to place such arbitrary power anywhere, much less in a mere medical board."

Continuing, the Court of Appeals dwelt at some length upon the general authority of medical boards, with particular reference to licensing by reciprocity. In this connection the Court said:

> "The whole action of the Board is based upon the fact that they have a different system of grading for admission to practice than that adopted by the Maryland Board. About the most inequitable test of ability that can be applied is the comparison of examination grades derived from either the same or different sources. It would certainly be dangerous to make arbitrary power dependent upon such a deceptive test. It is well settled that licensing boards are not vested with personal or arbitrary power, but are subject to the control of the courts when it appears that they have acted arbitrarily in refusing a license."

Concluding, the Court of Appeals said:

> "The answer of the Board totally fails to set forth any legal justification for its refusal to grant relator a license. . . . It was its duty to have acted favorably on the application. Refusing to do so, the relator availed himself of the only remedy afforded him and the court below should have sustained the demurrer and issued the writ."

The judgment of the lower court was reversed.

The case of *Czarra v. Board of Medical Supervisors* (24 App. D.C. 251) involved the meaning of the words "unprofessional or dishonorable conduct." Dr. Sigmund A. Czarra had been charged in the Police Court with having distributed obscene literature, and had forfeited collateral. Thereupon the Board of Medical Supervisors revoked his license. The Court of Appeals reversed the Board calling attention to the fact that it was incumbent upon Congress to define the meaning of "unprofessional or dishonorable conduct" and not leave the subject "to the possible caprice of any board of supervisors."

The Board of Medical Supervisors was more successful in the case of *Kemp v. Board of Medical Supervisors* (46 App. D.C. 173). Dr. Thomas J. Kemp had been convicted of violation of Sec.

211 of the United States Criminal Code. The Executive Committee of the Medical Society filed complaint charging Dr. Kemp with having been convicted of a crime involving moral turpitude, whereupon the Board, after due hearing, revoked his license and the Court of Appeals affirmed the Board.

Hutchins v. Hutchins (48 App. D. C. 495) was a will contest. While no medical man was a party, the case is of interest to the profession for it involved the interesting question whether a physician, who is incompetent to testify concerning confidential information acquired in his professional capacity, can express an opinion "based upon facts independent of the forbidden sources." In a will contest in the lower court Dr. Zachary T. Sowers, who had been testator's family physician for 37 years, was permitted to testify to conversations with testator and observations that he had made when making non-professional social calls. The Court enjoined upon this witness the duty of discriminating between competent and incompetent facts. This was held by the Court of Appeals to be in error, that Court remarking that "Such an opinion emerges from the mental processes of the witness without judicial scrutiny of the facts upon which it is based."

The cases which have here been referred to are not all of the medical and surgical cases that have been passed upon by the appellate court. In the interest of brevity some cases which did not include new or important legal interpretation have been omitted.

In conclusion, reference is made to *Bryant v. The District of Columbia Dental Society* (26 App. D.C. 461) which, although not a medical case, is the leading case in this jurisdiction on the right of corporations such as the Dental Society or Medical Society to expel members for failure to comply with the by-laws. A by-law of the Dental Society gave it authority to expel a member for "any act of special immorality or unprofessional conduct. . . ." In pursuance of the method prescribed by the by-laws, 4 members of the Dental Society charged Dr. Bryant with various acts of unprofessional and unethical conduct. It is interesting to note that one of the alleged acts of unprofessional conduct was that at a meeting of the Society he "characterized the members as being a lot of cats." After report of a committee to which the charges were referred, Dr. Bryant was expelled from membership, whereupon he applied for a writ of mandamus to compel the Dental Society to restore him to membership. The Supreme Court of the District of Columbia dismissed the petition for the writ and from that order an appeal was taken to the Court of Appeals.

The opinion of the Court of Appeals reviewed the entire matter in extenso. It called attention to Dr. Bryant's contention that the acts which were charged as constituting unprofessional conduct were not in fact unprofessional, with which contention the Court of Appeals did not agree. It held that the determination of what the Dental Society regarded as unprofessional conduct rested with the Dental Society and its determination would not be disturbed.

The opinion of the appellate court gave careful consideration to whether or not the accused had been accorded a fair trial by the Dental Society and came to the conclusion that regardless of the fact that the association did not hear all the evidence but took action upon its committee's report, its action was in full compliance with the by-laws. The Court of Appeals affirmed the decision of the lower court and this opinion has been quoted with approval in very many other jurisdictions.

Thoracoscopy and Intrapleural Pneumolysis. Report of 50 Cases.—There has been a marked tendency in recent years to broaden the indications of the use of artificial pneumothorax in the treatment of pulmonary tuberculosis. The presence of cavity, however, continues to be the most universal indication. Should pneumothorax fail to close the cavity within a reasonable time, continuance is not only useless, but the possibility of complications is enhanced. Inability to close cavity in a major percentage of cases is due to the presence of adhesions, and it is in these cases that one is tempted to use high pressure pneumothorax with the attendant danger of tearing adhesions, perforation of the lung, and empyema. Here, intrapleural pneumolysis is desirable and is indicated as soon as it is demonstrated that the cavity or cavities will not close under ordinary pressures. We feel also that pneumolysis should be performed in instances where an adhesion is directly over a large cavity even though the cavity be closed and the sputum negative for tubercle bacillus. In several of our cases, in which pneumothorax was induced prior to the use of cautery, upon re-expansion of the lung 3 to 5 years later, the cavity was found still open. The operation is not without risk and should be attempted only by a surgeon with skill and experience. . . .

Comment.—From an analysis of the above cases, we believe that intrapleural pneumolysis is a valuable adjunct to the use of artificial pneumothorax. This is in spite of the cases of empyema. In all 3, thoracoplasty would not have been possible because of bilateral disease.

Extract from article by HARVEY B. POWERS, M.D., Lake Kushaqua, N.Y., *New York State Journal of Medicine, March* 1, 1937, p. 482.

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RECENT DEVELOPMENTS IN TREATMENT OF CUTANEOUS ULCERS

Among many conditions which cause anxiety and exasperation both to the physician and the patient are stubborn skin ulcers and wounds. Much research work and a great deal of effort has been and is being expended to obtain methods and drugs to facilitate healing. Certainly, the development of the Elastoplast type of bandage, particularly in the treatment of ulcers due to varicose veins has been a boon to a great many sufferers. Douglas[1] in an admirable paper points out its great value not only in the varicose ulcer but also in the treatment of trophic, traumatic and syphilitic ulcers. He has also used this treatment in burns and decubitus ulcers. He believes that Elastoplast forms an excellent protective and semi-occlusive dressing for wounds which are not acutely infected. Further, it combines all the desirable properties of Unna's boot, the elastic stocking, gutta-percha tissue and ordinary adhesive without the disadvantages of any. However, one must not overlook the fact that treatment of the underlying condition is of paramount importance, and failures in treatment are often due to neglect in treating the fundamental cause.

Reimann[2] has reported very favorable results with the use of Thiocresol. He used the drug in a concentration of 1 to 10,000; this was applied to wounds for several days, and then bland treatment was used for several days, thus reducing skin irritation. Very distinct and definite healing occurred in wounds and ulcers very resistant to other types of therapy.

Cysteine will also bring about remarkable healing and skin growth in ulcers of long standing. Brunsting and Simonsen[3] of the Mayo Clinic demonstrated the use of Cysteine in 200 cases and showed excellent results. Dressings were held in place by a sponge incorporated in elastic bandage by which firm pressure was exerted.

The use of pancreas hormone is advocated by Schweitzer[4]. He points out that there have been many contradictory views on the use of this hormone, but he believes that it may be very helpful. Good results were obtained in a number of chronic ulcers, including one from X-ray burns. He used a salve composed of pancreatic ferment, 6.0; zinc oxide, 14.0; adeps lanae, 60.0; and jec.aselli, 20.0.

Allantoin, a product of maggot excretion and also of the urine of dogs, was found by Robinson[5] to exert all the beneficial action of the maggots themselves in the healing of chronic wounds, at the same time eliminating the disadvantages of maggot treatment. This substance is used in the strength of 2.5 grams of allantoin to 500 cc. of water or as an ointment. The solution is applied by means of wet dressings.

Recently, Azochloramid, a chlorine derivative, has come to the fore as an excellent drug in the treatment of wounds and ulcers. The formula is rather complex, N—N[1]—dichloroazodicarbonamidine, and it is distinguished from all other chlorine derivatives because of its slow rate of interaction with organic material, and its stability. Goldberger[6] reports that a specimen of azochloramid solution, 1 to 3,300, was allowed to stand in a 1,000 cc. flask exposed to daylight and to room temperature, and that at the end of a year the solution had lost practically none of its potency. Azochloramid comes in solution, 1 to 3,300, and also in Tri-acetin, 1 to 500. The tri-acetin preparation has greater solvent action on necrotic tissue and is preferable to the solution in the treatment of skin ulcers. The skin may occasionally be irritated by the continued use of Azochloramid, but this usually does not amount to much. Young[7] reports that Azochloramid is particularly effective in treating ulcerations occurring in patients with diabetes mellitus. Also after toe amputations in the presence of infection, healing was more rapid when Azochloramid in Tri-acetin, 1 to 500, was used.

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[1] Douglas, B.: Conservative and Radical Measures in the Treatment of Ulcer of the Leg; Study of Technics, Indications, and Results. Surg., Gynec. & Obst., 1935, **61**, 458.

[2] Reimann, S. P.: Use and Reasons for the Use of Thiocresol to Stimulate Wound Healing. J. A. M. A., 1930, **94**, 1,369.

[3] Brunsting, L. A., and Simonsen, D. G.: Cutaneous Ulcers Treated by Sulphydryl Containing Amino-acid Cysteine. J. A. M. A., 1933, **101**, 1,937.

[4] Schweitzer, A.: The External Application of Pancreas Hormone in Dermatology with Special Reference to Treatment of Ulcus Cruris and Roentgen Ulcer. Urol. & Cutan. Rev., 1936, **40**, 333.

[5] Robinson, W.: Stimulation of Healing in Non-healing Wounds by Allantoin Occurring in Maggot Secretions and of Wide Biological Distribution. J. Bone & Joint Surg., 1935, **17**, 267.

And finally, sympathetic ganglionectomy has been used a great many times in cases of chronic and trophic ulcers. A good deal of work is being done abroad, and in this country at the Mayo Clinic, and the results are certainly encouraging. Passive vascular exercises by means of alternating positive and negative pressures is another efficacious but also one of the less practical methods of curing chronic ulcers. Iontophoresis with theobromine compounds likewise has been found to be of value.

At any rate, with the passage of time and our slowly increasing knowledge of therapeutics, and with the development of new drugs and methods of treatment, the outlook in these discouraging cases is much brighter. Careful consideration of the fundamental pathology present and a combination of the proper general and local treatment will give a high percentage of cures.

S. D.

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[6] GOLDBERGER, H. A.: Treatment of Surgical Infections with Solutions of a New Chlorine Compound of Low Potential. West. J. Surg., 1936, **44**, 105.

[7] YOUNG, F.: The Treatment of Surgical Infections with New Chlorine Solutions. Surg., Gynec. & Obst., 1936, **63**, 318.

TRANSACTIONS OF THE SOCIETY

Stated Meeting, March 3, 1937

The following were duly elected to membership:

Active Members

Louis Bernard Bachrach, The Farragut Medical Building
Hugh Osgood House, 1835 Eye Street, N.W.
Robert Sterling McGrath, 1832 Eye Street, N.W.
Spencer Vincent Mead, 2205 Minnesota Avenue, S.E.
Stephen William Nealon, Jr., 1611 Twenty-first Street, N.W.
John Raymond Raedy, 21 N Street, N.W.
Duane Case Richtmeyer, 2015 Que Street, N.W.
Alfred Henry Richwine, 1365 Kennedy Street, N.W.
Francis Thomas Sharpe, 3323 O Street, N.W.

Associate Members

George Brackett Dowling, Alexandria, Va.
David Vincent McCauley, Ph.D., Georgetown University
Othmar Solnitzky, 109 East Thornapple Street, Chevy Chase, Md.
Genevieve Margaret Stewart, Saint Elizabeths Hospital

Reinstatement to Active Membership—Charles John Demas

Applicants for membership to be voted on in May, 1937:

For Active Membership

William Henry Beard, George Washington University—1933
Andrew Joseph Betz, Georgetown University—1929
Sterling Bockoven, State University of Iowa—1924
Warren Bernard Burch, Georgetown University—1931
Catherine Welch Johnson, University of Minnesota—1932
Ann Patrick Kent, University of Maryland—1933
Benjamin Paul Lafsky, George Washington University—1932
William Cornelius Lambert, Georgetown University—1932
Arthur Harry Lewis, George Washington University—1935
Paul Abraham Lichtman, George Washington University—1932
James Morgan Loftus, Georgetown University—1932
Barton Winters Richwine, George Washington University—1934
John Arthur Simpson, Georgetown University—1933
Albert McElroy Wheeler, University of Arkansas—1930

For Associate Membership

Robert Henry Detwiler, Georgetown University—1933
B. Edwin Erikson, D.D.S., George Washington University—1919
Howard Tilton Morse, College of Medical Evangelists—1929
Frederick Walters Norris, University of Texas—1924

Amendment to the Constitution Adopted

Substitute for Section 5, Article IV, Chapter IX, of the Constitution:

No member of the Society shall engage in any professional capacity whatsoever with any organization, group or individual, by whatever name called or however organized, engaged in the practice of medicine within the District of Columbia or within 10 miles thereof, which has not been approved by the Society.

The Executive Committee is authorized and directed to prepare an approved list of organizations, groups and individuals, by whatever name called and however organized, engaged in the practice of medicine within the District of Columbia or within 10 miles thereof, and the same shall be kept in the office of the Secretary-Treasurer. Before any such organization, group or individual can be placed on the approved list of the Society, such organization, group or individual, or the member of the Society proposing professional relations therewith, shall submit to the Compensation, Contract and Industrial Medicine Committee such evidence as the Committee or the Society may require showing the character, activities, financial condition and ethical standards of said organization, group or individual, and after considering the same, said committee shall make a report of its investigation and findings to the Executive Committee for such action as it may deem necessary.

Nominating Committee Elected

Pursuant to Chapter VI, Article II, of the Constitution,* a Nominating Committee was elected by the Society to select nominees for each elective office. The personnel of the committee is as follows:

Fred R. Sanderson, *Chairman*
John H. Lyons
Sterling Ruffin
Edgar M. McPeak
John B. Nichols

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* The Nominating Committee shall select a nominee for each elective office and elective committee vacancy for the following fiscal year or years as hereinafter provided. At least 4 weeks prior to the annual meeting it shall file its nominations with the Secretary, who shall immediately publish the report of the Nominating Committee to the membership of the Society. Other nominations may be made, provided that such nominations are signed by 10 members in good standing and are filed with the Secretary at least 2 weeks prior to the annual meeting. The Secretary shall send a copy of all nominations to the membership at least 1 week prior to the annual meeting. In the event of their being no quorum at the annual meeting, those nominated by the Nominating Committee shall take office in the same manner as though duly elected.

COMING MEETINGS

Friday, March 26: *The Section on Internal Medicine.*
"The Evaluation of Medical Therapy of the Upper Gastro-intestinal Tract." Henry A. Monat, M.D.
Election of officers.

Wednesday, April 7: Business Meeting of the Society. Reports of committees, etc.

Wednesday, April 14:

1. "Nose and Throat Manifestations in the Acute Infections of the Mononucleosis Type." George B. Trible, M.D.
2. "Renal Tuberculosis." Ralph M. LeComte, M.D.

Friday, April 16: *The Section on Ophthalmology & Otolaryngology.*

1. "A Trip to Vienna." Fordyce A. H. Johnson, M.D.
2. "Case of Petrositis, With Recovery." E. G. Breeding, M.D., and H. H. Schoenfeld, M.D.

Wednesday, April 21: Joint meeting with the Section on Internal Medicine.

Wednesday, April 28: Presidential Address. Buffet Supper.

ANNUAL SCIENTIFIC ASSEMBLY

May 5–6

These meetings, which have annually for the past 9 years been largely attended by our own members and numbers of out-of-town guests, have filled a special function in presenting from the abundant clinical resources of the Nation's Capital postgraduate instruction of exceptional value. A complete program of the coming meetings will be ready for release on March 15. Included will be papers by visiting speakers in surgery and medicine. Dr. James C. White, Assistant Professor and Tutor in Surgery, Harvard Medical School, will read a paper, "The Sympathetic Nervous System in Relation to Cardiovascular Disease." Associate members, Drs. Jacob W. Bird and Sanford M. Rosenthal, will be heard, the former on "The Operation of a Small Community Hospital," the latter on "Chemotherapy of Bacterial Infections with Sulphonamine Compounds." An opportunity is given the profession of Washington and its environs for all registrants to meet at the noon day complimentary luncheon to be held at the Mayflower Hotel for friendly contacts. A brief address is made usually by a nationally known lay figure.

Francis G. Blake, M.D., a Guest Speaker

Dr. Blake, Sterling Professor of Medicine, Yale University, will speak on "Serum Therapy in Pneumonia." Thirty or more other noted local teachers and scientists will present articles on subjects such as the latest developments in heat therapy; use of mandelic acid, Prontosil and Prontylin; and on other interesting and practical phases of practice.

Howard Wilcox Haggard, M.D., Addresses the Public Meeting, Evening of May 5

Scientific Exhibits, Technical Exhibits

There will be many interesting and instructive exhibits.

The Medical Society of Virginia, Maryland and District of Columbia meets concurrently with the Medical Society of the District of Columbia on Wednesday, P.M. Washington is noted as a National Clinical Center. Do not fail to record the dates. Plan to attend. There are no registration fees.

Second Annual Postgraduate Institute of the Philadelphia County Medical Society will be held April 12–16, 1937, at the Bellevue-Stratford Hotel, Philadelphia. The subject: "Diseases of the Chest and Upper Respiratory Tract." Registration fee, $5.00. Members of the Philadelphia County Medical Society admitted without charge. Among the guest speakers are noted: The Honorable S. Davis Wilson, Mayor of the City of Philadelphia; Dr. Frederick J. Bishop, Reading, President-elect, Medical Society of the State of Pennsylvania; Dr. J. Shelton Horsley, Richmond, Va. Over 55 separate presentations will be made. Drs. George E. Pfahler, Chevalier Jackson, Louis H. Clerf, David Riesman, and William D. Stroud, are included among essayists. Write to the Philadelphia County Medical Society, 21st and Spruce Streets, Philadelphia, Penna., for complete program.

American Neisserian Medical Society, third annual meeting, will be held on June 8, 1937, at Atlantic City, N. J. The program will consist of papers and discussions on the various phases of the management and control of gonorrhea. All who are interested are cordially invited to be present.

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS

The regular meeting of the Washington Society of Pathologists was called to order at 1:30 P.M., February 6, 1937, in the Army Medical Museum by the President, Dr. Roger M. Choisser. The minutes of the meeting of January 9, 1937, were read by the Secretary, Captain Elbert DeCoursey, and approved. Drs. Harry S. Bernton and Henry L. Wollenweber were unanimously elected as associate members in the Society. Drs. H. H. Hazen, L. E. Burney, C. T. Carroll, and Alfred Blumberg were guests.

Scientific Paper

"Analysis of the Results of 20,093 Triple Serologic Tests for Syphilis (Kahn, Hinton and Wassermann); Including Initial Triple Tests on 16,997 Successive Cases on Admission to the Hospital." **Laurence C. Milstead, M.D.,** Pathologist, Sacred Heart Hospital, Allentown, Penna.

Charts were portrayed which indicated the results of triple tests performed at the Sacred Heart Hospital, Allentown, Penna., during the 7 years and 5 months' period between June 1, 1929, and October 31, 1936.

The objects of the presentation were:

1. To show that a method of representing triple results by 3 initials is simple and expedient.

2. To show that consideration of the combined result of a triple test is of greater value than consideration of the isolated results of individual tests in the serodiagnosis or the sero-exclusion of syphilis.

3. To indicate the percentage incidence of seropositive syphilis in 16,997 successive hospital admissions.

The false positive expectancy and the positive incidence in various groups of the triple test were demonstrated, and an effort was made to integrate the results rather than to consider the 3 tests separately. It was shown that a consideration of the combined results of the triple tests gives a more trustworthy picture of the patient's status with regard to syphilis.

The tabulations included:

1. Successive admissions to the hospital	16,997
2. Accession and dispensary cases	3,096
3. Total tests	20,093
4. Successive admissions to the maternity service	2,853
5. Successive admissions to the pediatric service	901
6. Tests in 409 cases of known syphilis	1,063
7. Initially false positive or doubtful reactions	567

All tests were tabulated as Positive (P), Doubtful (D), or Negative (0). The triple test results were indicated by 3 initials placed successively: The first initial represented the Kahn result, the middle initial represented the Hinton result, and the final initial represented the Wassermann result. With 3 tests performed and 3 possible results for each test there was a total of 27 categories listed. By comparing the results in these categories in the 16,997 successive admissions to the hospital with identical categories in the known syphilis group and the false positive group it was possible to work out the false positive incidence and the false positive expectancy in terms of the routine tests on admission to the hospital.

The false positive expectancies for various groups of results in the triple test were given as follows:

3–P	False Positive Expectancy	0
2–P 1–D	" " "	2 in 100
2–P 1–O	" " "	7 in 100
1–P 2–D	" " "	1.4 in 100
1–P 1–D 1–O	" " "	10.6 in 100
1–P 2–O	" " "	56 in 100
3–D	" " "	46 in 100
2–D 1–O	" " "	62 in 100
1–D 2–O	" " "	over 75 in 100

The false positive expectancies of these categories of the triple test were compared with the strong positive Kahn tests, Hinton tests and Wassermann tests which occurred in the group of 567 patients showing an initial false positive or doubtful reaction who were negative on retesting and who gave no signs or history suggestive of syphilis. Of this group 9.34 per cent gave false positive Wassermann results, 7.24 per cent gave false positive Kahn results, and 6.34 per cent gave false positive Hinton results.

The incidence of seropositive syphilis for the 16,997 successive admissions to the hospital as well as for the successive admissions to the maternity and pediatric services was given. For the total hospital admissions the absolute incidence (3-P) was 3.09 per cent, the very highly probable incidence was 1.82 per cent, and the total incidence was 4.91 per cent. For the maternity service the absolute incidence (3-P) was 1.29 per cent, the highly probable incidence was 0.99 per cent and the total incidence was 2.28 per cent. For the pediatric service the absolute incidence (3-P) was 0.99 per cent, the highly probable incidence was 0.27 per cent, and the total incidence was 1.26 per cent. Negroes comprise less than 0.2 per cent of the admissions to the Sacred Heart Hospital.

DISCUSSION

Dr. H. H. Hazen of the United States Public Health Service: I congratulate Dr. Milstead on a number of points which were brought out in the presentation of his paper, namely, he showed very clearly the need for multiple tests for syphilis, stating that too many physicians all over the country depend too much on the results of the one test alone. I congratulate Dr. Milstead upon developing a finger blood test. We need more than one test if we are going to use blood from children. In the third place, I wish to congratulate Dr. Milstead for having utilized the services of the evaluation committee to check up his results.

Dr. L. E. Burney stated that when these tests are performed for malaria, tuberculosis, or leprosy, they are performed in numerous laboratories in such a varied way that there is a large degree of error in the performance of these tests. In the evaluation they are either not carried out as in the Kahn and Hinton tests, but short cuts are used so that the various laboratories do not get the same results. Secondly, the necessity of doing routine serological examination on all outpatients in hospitals should be stressed. About 66 per cent of the patients do not know that they have syphilis, and had never been treated for syphilis. By taking routine tests in 3,000 private patients it was found that 10 per cent of these private patients had positive serological tests for syphilis. In another group it was found that 35 per cent of the patients with syphilis with less than 4 years' duration gave no history of any symptoms of syphilis. When you have a large number of patients who do not know they have syphilis, the necessity for doing routine examinations on patients cannot be emphasized too much.

Dr. E. Clarence Rice asked Dr. Milstead what were the criteria for a "known" syphilitic patient.

Dr. H. H. Leffler: I think this is a very interesting paper and brings out the point which I have so often felt should be brought out, i.e., multiple tests rather than single tests. When you run both Kahn and Wassermann tests, which I did for several years until I had to give it up and do one or the other, it was quite frequently very puzzling to decide which system to believe. Lately we have had to depend entirely on the Kahn test because of lack of skilled technical help to carry out the reactions. We run 60 to 80 Kahn's every day, and with 1 person cannot do other tests in addition. I was very much interested in Dr. Milstead's low percentage of positives compared with the percentage we have in Gallinger Municipal Hospital. It is very likely that our great number of colored patients brings up the percentage.

Dr. Milstead (closing): I want to thank all of the participants in the discussion. In answer to Dr. Rice, I can also refer to Dr. Leffler's discussion and say that to evaluate our positive cases is quite a problem in our city because we do not have much secondary syphilis coming into the hospitals, probably not more than 15 per cent, and I am sure that I have not had more than 20 per cent positives, probably because the patients have been coming back and have been showing positive reactions time and time again.

Presentation of Cases

Dr. Harry A. Davis presented the gross specimen of an unusual aortic thrombus from a white male, 57 years of age, who was admitted to the hospital complaining of heaviness in both legs which began a few hours previously during an attack of coughing. The patient's health had been excellent previously. There was no known predisposing cause. Bilateral gangrene of the legs developed. At autopsy a bilateral thrombosis of the iliac arteries was found and also a loose thrombotic tag adherent to the aorta just above the aortic valve leaflets.

In the discussion it was generally considered an embryologic defect, although arguments against this concept were offered.

Dr. H. E. Ragle presented a case of a young man, about 33 years of age, from whom a lymph gland had been removed from the right side of the neck about 4 years before. About a year ago he had 2 tumor masses appear in the right subaxillary region. These 2 masses, about the size of walnuts, were removed.

In the discussion, the diagnosis of mixed tumor of a salivary gland was the consensus of opinion. One member considered the prognosis as poor.

Dr. Oscar B. Hunter presented a case of a young man, aged 32 years, whose only illness with the exception of the usual diseases of childhood had been in 1923 or 1924. He was considerably under weight and his appetite was poor and complexion was sallow. He was unable to gain weight. Several tests were made at that time for tuberculosis and he was put in a tent in San Diego for some time. It was finally decided that he did not have tuberculosis. In 1923 or 1925 he had deviation of the nasal septum which was about the only finding up to the last illness. In October, 1935, while driving he noticed considerable swelling in the neck and in 3 or 4 hours the pain became very severe. His tonsils were removed and he improved considerably. His condition did not improve satisfactorily and he was taken to Garfield Memorial Hospital where a small gland was removed from his neck. At the present time he has a swelling of the glands of his neck. The blood count on October 28, 1936, was: R.B.C., 4,000,000; W.B.C., 6,200; Hgb., 80 per cent; December 8, 1936: R.B.C., 4,160,000; W.B.C., 10,400; Hgb., 82 per cent; January 5, 1937: R.B.C., 3,750,000; W.B.C., 7,700; Hgb., 70 per cent; January 28, 1937: R.B.C., 4,190,000; W.B.C., 7,500; Hgb., 75 per cent.

In the discussion, most members thought that the histopathologic picture was that of inflammation; however, some were not sure that a tumorous process was not present.

Dr. Hunter presented also the case of a young child, 3½ years old, with a history of severe pains in the bones. On December 28, 1936, the red cell count was 2,000,000; Hgb., 42 per cent; January 4, 1937, the red cell count was 2,930,000; Hgb., 57 per cent; January 12, 1937, the red cell count was 3,500,000; Hgb., 58 per cent; January 18, 1937, the red cell count was 3,030,000; Hgb., 49 per cent. She was treated at Children's Hospital, and a number of transfusions were given during this time. A lymph gland was taken out; part was ground up and inoculated into a brain culture, and a nonhemolytic streptococcus was obtained. The child has very large tonsils which are definitely infected.

Dr. C. T. Carroll added that the past history was negative except that she was more or less of a hyperplastic type with small bones, poor appetite and poor color. Her present illness began about December 1 with an attack of abdominal pain, tenderness and rigidity of muscles, and fever. Her tonsils were not examined at that time. The temperature ranged from 101°F. to 104°F. She was able to be up and around in 3 or 4 days, and then there were intermittent low grade irregular fever and increase in pallor. She complained of pains in her bones, chiefly in her arms, legs and fingers. At that time there was evident tonsillitis with enlargement of the tonsils and enlargement of the cervical glands. The other glands were not enlarged. There was no enlargement of the spleen or liver. She remained about the same until about December 22, when her temperature rose to 104°F. or 105°F., and remained at 101°F. to 105° F. for about 10 days. At this time her tonsils were very bad in appearance, although there was no exudate. She was taken to the Children's Hospital and had 2 small transfusions. The temperature dropped to normal for about 2 weeks, although during that time she complained of abdominal pains and pains in the fingers. She had another acute flare-up of tonsillitis which lasted 4 days. At this time the tonsils showed a definite exudate of pus and blood. After this, pentnucleotide was administered and she went to the hospital for biopsy and 3 small transfusions because the red blood count was beginning to drop. After the second transfusion she developed a blotchy appearance over her face and upper part of her thighs. The blotches were erythematous and resembled measles except that they were larger and tended to become confluent. Three or 4 days later she developed an acute infection in the tarsal conjunctiva of the right eye which subsided after treatment, and 3 more small transfusions were given with more pentnucleotide. The red blood count was down to 3,000,000 and at that time daily doses of pentnucleotide and liver extract were given and continued up to the present time. Now there are numerous pustules on the face and one on the cheek which apparently is going to be an abscess. The doctors have thought the pains in her legs are leukemic symptoms. The only point which I wish to stress is that she had had no fever at any time without demonstrable infection somewhere.

Dr. E. Clarence Rice said that about 3 weeks ago the patient had a blood examination at which time her white count was low, her red blood count was down considerably, and her poly's were around 10 per cent. She had an excess of young lymphocytes and a number of lymph glands. Red blood cells showed no definite abnormalities. Following a blood transfusion her red blood cell count came up to normal; her white count did not change perceptibly, in fact it went down, the reticulocytes remaining the same. The number of lymphocytes increased so that at times there were about 100 per cent. Lymphoblasts were present up to 18 per cent. These cells were practically oxydase negative. An occasional myeloblast was seen, but at the last count the poly's did not exceed 10 per cent. The red blood cells show practically no change at all. Her total red count as a whole remained fairly normal. It has been his feeling that the child had an aleukemic phase of a leukemia. Quite a number of such cases have been in the hospital from time to time, and at present there are 2 or 3 in the building. A bone marrow puncture has not been done. The diagnosis seems to lie between an infectious condition, as Dr. Hunter stated, anaplastic anemia possibly due to the reaction of the infection, or a leukemia with the positive reaction of the infection. However, from his past experience he would be inclined to the diagnosis of leukemia, although in a section such as this he would not hold out for a positive diagnosis.

In the discussion it was thought that the histologic study revealed no more than an inflammatory picture. It was wondered if this one lymph node were an index as to what was actually happening in the patient.

Dr. J. W. Lindsay presented 2 microscopic slides from the uterus, 1 taken about 3 months before the second, irradiation by radium implantation of the uterus having occurred in the interim.

Dr. Lindsay presented also a slide from the case of a breast which was removed after irradiation on the basis of a clinical diagnosis of cancer. The section was taken from the wall of the cyst after the breast was removed.

In the discussion it was said that fat necrosis in the breast was all that could be said from the microscopic section; but that cancer nests would possibly if not probably be found in serial sections.

Dr. L. L. Ashburn presented first the case of a white man, aged 68 years, who gave a history of frequent nocturia and dysuria for a year prior to admission without pyuria, hematuria or perineal pain. There was no evidence of bone involvement of the pelvis or spine. On admission the prostate was found to be stony hard and of moderate size. The urethra at the neck of the bladder would admit only a very small catheter. There was a residual urine of 8 ounces. Prostatectomy was performed, the prostate being peeled out with difficulty and in small portions. In areas it appeared to be calcified. Histologically the specimen showed the usual picture of adenocarcinoma. The stony hard nodule was composed of myxomatous, cartilaginous, and caseous tissue, intimately associated with tumor cells.

In the discussion it was pointed out that bone could form in old sebaceous cysts, in genito-urinary epithelial transplants and in the lungs.

Dr. Ashburn presented also the case of a white man, aged 59 years, who showed at autopsy a fungating, necrotic flat growth involving roughly 75 per cent of the urinary bladder. The clinical history together with autopsy was presented at the last meeting. At that time the diagnosis of leiomyosarcoma of the bladder did not meet with complete agreement, Dr. H. H. Leffler and Captain Elbert DeCoursey being the only ones who thought this was definitely sarcomatous. The autopsy tissues fully confirm the leiomyomatous nature of the tumor.

Dr. R. D. Lillie presented a section from a brain tumor of which a classification of spongioblastoma multiforme had been made. The fibrillary matrix in astrocyte areas was shown in the slide.

Dr. R. M. Choisser presented the case of a tumor removed from Poupart's ligament of a white woman, aged 50 years. She had noted a tumor below the left ligament 2 years ago. It has gradually enlarged to the size of an olive. The general health is good. There are other enlarged glands. This one was shelled out easily.

In the discussion the diagnoses of benign neurofibroma, fibrosarcoma, and neurogenic sarcoma were given.

Dr. Choisser presented also the case of a white woman, aged 30 years, who had enlarged cervical lymph nodes of 3 weeks' duration. The largest node was the size of a small bean. There was no local evidence of infection. These nodes were somewhat painful when first noted and were believed to be inflammatory, but no foci of infection could be found. It may be a lymphoblastoma, or it may possibly be inflammatory, but from the type of reaction, mitosis within the medullary cords and proliferation of the reticulum it is probably an acellular Hodgkin's disease.

In the discussion the opinions favored the diagnosis of early Hodgkin's disease.

The meeting adjourned at 4:40 P.M.

NEWS AND PERSONALS

Dr. Wallace M. Yater read a paper, by invitation, on the evening of March 1, 1937, before the Hartford Medical Society, Hartford, Connecticut. Subject: "Histopathologic Basis of Auriculoventricular and Intraventricular Conduction Disturbances." On the afternoon of the same day he held a clinic at St. Francis Hospital, Hartford, on "Pleriphera Vascular Disease."

The Annual Banquet of the Jacobi Medical Society will be held at the Shoreham Hotel, Saturday, April 3, 1937. Dr. A. S. Hyman, of New York, City, has been selected as the guest speaker.

Dean E. B. McKinley, George Washington University School of Medicine, delivered an address before the Chinese Medical Association in Shanghai, on February 5, 1937. Later he visited Hongkong. It will be recalled that Dr. McKinley is on sabbatical leave in connection with his studies on leprosy in the Philippine Islands.

The George Washington University School of Medicine Postgraduate Course in Ophthalmology will be given May 31–June 6, 1937, inclusive. The lecturers include: Drs. Clyde C. Clapp, Robert Von der Heydt, Arthur J. Bedell, Sanford R. Gifford, Harry S. Gradle, S. Hanford McKee, S. Judd Beach, LeGrand H. Hardy, P. Chalmers Jameson, Edward Jackson, and Walter B. Lancaster.

The Smith-Reed-Russell Lecture, George Washington University School of Medicine, will be given on March 18, 1937, by J. G. Townsend, M.D., Director of Health, Office of Indian Affairs, United States Department of Interior. Subject: "Medical Activities Among the Beneficiaries of the Indian Service."

William Alanson White, (1870–1937)

CAT.

William Alanson White, M.D., M.A., D.Sc., LL.D.

1870–1937

Dr. William A. White, of world-wide reputation as an outstanding psychiatrist, teacher and author, who became a member of the Medical Society of the District of Columbia by invitation through action of the Board of Censors in 1906, died on March 7, 1937. Dr. White's membership by invitation was phrased, according to the Society's record of April 25, 1906, as follows:

> "In view of the high personal character, literary and scientific attainments, and eminent position of Dr. William A. White as Superintendent of the Government Hospital for the Insane, we, the undersigned, respectfully recommend that he be made a member of the Medical Society of the District of Columbia, by invitation."

and was signed by 16 members.

Since his coming to Washington in 1903, as Superintendent of Saint Elizabeths Hospital, in which position he demonstrated unusual ability as an executive, Washingtonians, both laymen and members of the medical profession, have had frequent opportunities of listening to his clear and effective speaking and of being able to profit by his ability to impart information. His many students at George Washington University and Georgetown University were fortunate indeed to have been recipients of his clear expounding of advanced psychiatric knowledge and above all to have known him as a friend. He was in special demand for speaking at medical gatherings; always was he willing to respond. Of special importance were his addresses to the public which were filled with calm reasoning expressed in simple language. "Relation of the Physician to the Public," "The Responsibility of the Citizen for the Health of His Community," "The Dependence of Modern Civilization Upon Health," were types of subjects discussed before lay gatherings sponsored by the Medical Society of the District of Columbia. Upon invitation, on the occasions of the dinner in honor of the late Dr. Samuel Shugert Adams' seventieth birthday, and the memorial meeting to the late Dr. John A. Foote, he delivered addresses which were fine examples of expression of eloquent sentiment and typified his coöperation on many similar occasions. Dr. White was an untiring scientific investigator and a prolific writer. Appended is a bibliography which shows that he has published some 109 essays and was the author of 19 scientific volumes. He was, jointly with Dr. Smith Ely Jelliffe, editor of "The Psychoanalytical Review."

Dr. White was graduated from the Long Island College of Medicine in 1891. He had received the honorary degrees, D.Sc., from Boston University and Washington University (Saint Louis); M.A., from Georgetown University; LL.D., from George Washington University. Among his memberships in scientific bodies are noted: American Medical Association, American College of Physicians, American Neurological Association, American Psychoanalytical Association, American Psychiatric Association, Association for Research in Nervous and Mental Diseases, American Psychopathological Association, etc. He was a founder, becoming the first president of the Washington Academy of Medicine, and was also President of the Social Hygiene Society and the Washington Institute of Mental Hygiene. He was a member of the Cosmos, Chevy Chase and National Press Clubs.

Dr. White is survived by his widow, Mrs. Lola P. White, and a brother, Charles H. White of Boston.

Funeral services were held at the All Soul's Unitarian Church on Wednesday, March 10, 1937. Of the honorary pall-bearers are noted: Drs. William M. Ballinger, Walter A. Bloedorn, George W. Calver, Ross M. Chapman, Hugh S. Cumming, Edward Y.

Davidson, Mr. F. A. Fenning, Drs. Ernest E. Hadley, Custis Lee Hall, General Frank T. Hines, Drs. William H. Hough, Oscar B. Hunter, Smith Ely Jelliffe, William J. Mallory, Cloyd Heck Marvin, William Gerry Morgan, General Charles R. Reynolds, Drs. William M. Sprigg and Lewis H. Taylor.

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CORRESPONDENCE

February 24, 1937.

Editor,
Medical Annals of the District of Columbia,
Washington, D. C.

Dear Sir:

Since publishing my article on the life of William C. Borden,* I have received a letter from General J. R. Kean, Retired, a part of which I request you to publish in the Medical Annals to clarify statements obtained by me from my father's personal records.

General M. W. Ireland, Retired, former Executive Officer to Surgeon General O'Reilly, has approved the facts submitted in General Kean's letter and I gladly submit this additional information.

Very truly yours,
(Signed) Daniel L. Borden, M.D.

2804 N Street, N. W.,
Washington, D. C.,
February 9, 1937.

My dear Dr. Borden:

I want to thank you for sending me your fine sketch of your father's career, both in the Medical Corps and afterwards as Dean and reorganizer of the George Washington University Medical School. It is a record of an able and industrious man who accomplished much original work and some great works which will long live after him and make his name remembered.

I regret to add that you have made claims in statements on page 7, referring to the Bill to Reorganize the Medical Department and the Creation of the Medical Reserve Corps, which are not in accordance with the facts. This I am sure has been done unintentionally through a misconception of your father's memoranda.

It is certainly not true as can be readily established that Colonel William C. Borden was the originator of the Bill to Reorganize the Medical Corps of the Army—nor did he originate the idea of the Medical Reserve Corps. The three assistants to General O'Reilly during the years when these things were accomplished are all yet living and can testify to this. It is a fact that Colonel Borden was an intimate friend of General O'Reilly and was consulted by him and his assistant during the five years' struggle to get the legislation past the General Staff and through Congress and gave valuable suggestions, but he was certainly in no sense the originator of the ideas contained in it. In fact he was rather opposed to the pushing of the Medical Reorganization Bill by the Surgeon General's Office because he was not optimistic as to its success and feared that it might interfere with the prospects of his General Hospital Bill.

The inception of this legislation was a paper, which we called the Brief, which was prepared by me as Executive Officer of the S. G. O. in the latter part of the year 1903, signed by General O'Reilly and handed to the Secretary of War, Mr. Elihu Root, on Christmas Eve of that year. When I went with General O'Reilly to a reception given by Mr. Root to the incoming Secretary, Mr. Taft, on New Year's day, Mr. Root told General O'Reilly that he had been entirely convinced by the Brief and he would do all in his power to promote the legislation needed by the Medical Department.

This Brief was the basis for the Medical Department Bill above referred to and contained all its important provisions. Your father doubtless had a hand in the final draft of the Bill and it was probably a copy of this final draft that you found among Colonel Borden's papers.

When the Bill became a law in April, 1908, the Medical Officers stationed in Washington had a dinner at the Raleigh Hotel to celebrate it. General O'Reilly at this dinner gave a history of the inception and progress of the Bill and sent a cable to me in Havana (I was then Health Officer of Cuba) congratulating me as its author. General Ireland was one of those present and can corroborate these statements.

As regards the defense of the Medical Reserve Section of the Bill against the attack of Dr. Azel Ames at the Saint Louis meeting of the Military Surgeons, in 1905, I recall it very distinctly. It was naturally my duty as the Executive Officer of the Surgeon General to make this defense but I asked Colonel Borden to do so as I was a poor and ineffective speaker and he a very calm, clear and effective one. The S. G. O. had circulated a draft of it for comment and Dr. Ames, who was mentally unbalanced and died insane not long after, submitted a very elaborate plan and got the idea that he had originated the entire scheme. He, therefore, made a violent attack upon the Surgeon General's Office for its failure to adopt his scheme. It was this attack and Colonel Borden's fine answer to it, which were published in the Military Surgeon in 1905.

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* See "William Cline Borden, 1858–1934," September and October, 1936, issues, M. Ann. District of Columbia.

Yours very sincerely,
(Signed) J. R. KEAN.

The District of Columbia Chapter of the American Red Cross acknowledges donations from members to the Flood Relief Fund:

February 23, 1937.

Dr. W. M. Sprigg, President,
Medical Society of the District of Columbia,
Washington, D. C.

My dear Dr. Sprigg:

Your letter of the 17th instant to General Frank Keefer, Chairman of the District of Columbia Chapter, has been passed on to me for my information.

The Medical Society has contributed handsomely to the President's appeal on behalf of the flood sufferers on the Ohio and Mississippi. I am proud of the Society in its humanitarian effort and want to thank its members that gave to the Fund upwards of $2,000.00, in support of the flood relief work which the Red Cross is now carrying on in this greatest emergency of modern times.

Please accept my congratulations and sincerest thanks for the helpfulness of the Society and its members.

Cordially yours,
(Signed) CARY T. GRAYSON
Chairman, Central Committes.

February 19, 1937.

Dr. C. B. Conklin, Secretary,
Medical Society of the District of Columbia,
Washington, D. C.

My dear Dr. Conklin:

Doctor Sprigg, President of your Society, personally conducted yesterday to my office, sums of money in cash and checks aggregating $1,049.25, these being gifts of Medical Society members in behalf of victims of the great flood. The amount cited, added to those previously contributed by members of the Society, makes the handsome total of $2,095.25. I enclose a receipt and request that you will convey to the Society, at the first opportunity, the warm thanks of the officials of this Chapter of the Red Cross. Admiral Grayson and the other officers of the National body have been advised of your generous action.

Very sincerely,
(Signed) F. R. KEEFER
Brig. Gen., U. S. Army, Retired.
Chairman, Executive Committee.

Communication received from the Health Officer, District of Columbia on March 4, 1937:

Special Notice

February 26, 1937.

FROM: The Superintendent, Pennsylvania State Police.
Harrisburg, Penna.

TO: The Secretary, Department of Health, of all States.

SUBJECT: Warning against an impostor.

It is reported from Detroit that a man posing as a clinical pathologist is visiting physicians there asking them to endorse checks to pay for repairs to his automobile. He called on one physician, who entertained him for a day and night, during which time he discussed clinical pathology without betraying himself. On the second day he looked at automobiles appearing to be disgusted with his old one. Later he left his host, saying he wished to go to a bank, but returned shortly, saying that the bank demanded identification. When the Detroit physician said he could not identify him, the visitor exhibited a bank book with a balance of $678.00. The physician then cashed a check for $50.00 on the Huntington National Bank, Columbus, Ohio. After an hour or more the "clinical pathologist" went out for a shave but telephoned that the Packard service agency was to pick him up and he would telephone later. That was the last heard of him. The Packard station reported they had no car for such a person and the Columbus bank reported it had no account for the man, who called himself Brown, and was about 5 feet 9 inches tall; dark brown wavy, wiry hair, a high forehead, dark skin, large brown eyes; thick skin with deep wrinkles; teeth excellent and very white; weight about 170 pounds. He wore a dark brown suit with pin stripe, an overcoat of Oxford gray and light felt hat.

You are respectfully requested to warn hospitals and physicians to be on the lookout for this man.

(Signed) Lynn B. Adams
Superintendent of State Police.

Note, Ed.—On March 5 a man of similar description and using about the same story is said to have visited at least 2 offices of local physicians and 1 dentist. Total known loss $55.00. All take notice—assist in bringing this man to justice.

MEDICAL DEFENSE

Dues

Have you paid your 1937 dues? If you do *not* wish to allow yourself to become delinquent and as a consequence to miss benefits of provisions of the Constitution, written in Chapter VII, Article IV, Section 5, send your check for $20.00 before midnight March 31, 1937. The members of the Medical Defense Committee, Drs. L. H. Reichelderfer, *Chairman*; Francis R. Hagner, John B. Nichols, and Coursen B. Conklin, *ex-officio*, are hopeful that no one this year will be deprived of the benefits through failure to heed this notice.

MEDICAL ANNALS
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VOLUME VI APRIL, 1937 NUMBER 4

PRESENT KNOWLEDGE ON THE RHYTHM OF HUMAN FERTILITY*

SOME BIOLOGICAL AND PHYSIOLOGICAL CONSIDERATIONS AFFECTING ITS PRACTICAL APPLICATION TO PROBLEMS OF STERILITY AND BIRTH CONTROL

PRENTISS WILLSON, M.D.
Washington

The last few years have witnessed a truly phenomenal increase in our knowledge concerning the physiology of human conception. The evidence of experimental and comparative biology, supported by clinical observations as well, now lends an ever-increasing support to the contention that this occurrence, that is, the actual union of sperm and egg, is only possible for a period certainly less than 24 and probably less than 18 hours in any menstrual cycle, and that intercourse, in order to be fertile, must take place not more than 48 hours preceding the actual accomplishment of ovulation. This theory of the physiology of human reproduction is obviously so revolutionary, so at variance with all previous ideas, both lay and medical, that, if true and susceptible of practical application, it renders the dissemination and popularization of any such knowledge a matter of concern not alone in the field of medicine, but also in the spheres of sociology and economics, morals and religion. For these reasons it has been felt that the presentation of some of its more important aspects might not be without interest. The subject will be presented in two parts: it is proposed, first, to consider the ascertained physiological and biological facts supporting the theory, the methods now devised for its practical application in medical practice, and the evidence such application has afforded of its susceptibility to successful clinical employment; and, second, to point out certain fundamental and basic factors that must be taken into consideration in undertaking to apply this or any other present or future knowledge to the moral, social or medical problems inherent in an attempt either to promote or control human fertility.

It is first necessary, however, to dispose of one fundamental objection that is frequently urged against the whole theory of a rhythm of sterility and fertility in woman. Its opponents maintain that if there were such a rhythm, and if it were definitely determinable, the common experience of mankind would have solved the problem of contraception at an early stage in the acquisition of human knowledge. This contention is sufficiently plausible to merit some detailed consideration. With the possible exception of the llama, camel, and rabbit, the females of species of subprimate rank in the phylogenetic scale are not only uninterested in the sexual advances of their males, but refuse them entirely, except during a brief period when, because of the imminence of ovulation, conception is possible. This biological moral standard, if one may so term it, makes it possible to determine the reproductive rhythms of these animals by observing their breeding habits and sexual behavior, and immediately discloses the enormous variations that characterize them. In many species the period of heat, rut, or estrus is a single annual phenomenon; in others, in the absence of conception estrus reappears at short intervals for a brief period of each year, to be followed by a prolonged anestrous cycle until the breeding season of the next year; others are polyestrous, estrus consistently following estrus at short intervals, unless the cycle be temporarily suspended by pregnancy, until permanently terminated by senility. Woman, and all of the higher primates, have apparently lost all trace of an annual breeding season, if such ever existed, and are definitely and continuously polyestrous. And, significantly, in woman, ape, and monkey, the rhythmical periodicity of the ovulatory cycles is at approximately monthly intervals. The sexual behavior of primate males, including man, is characterized by a continuous sexual activity and reproductive capacity that, however, is observed in the males of many other species of lower phylogenetic rank, while primate females, on the other hand, differ from those of practically every other species except possibly those mentioned above, in displaying continuous receptivity to sexual attention. There can be no question that desire on the part of primate females is increased at the time of ovulation, but it is also more or less subject to appropriate stimulation during any phase of the menstrual cycle, and even during pregnancy itself. Thus the time of estrus in women long escaped recognition because, during it, characteristic differences in their sexual behavior are not sufficiently marked to have attracted attention; and this fact naturally led to the popular conclusion that this type of sexual behavior on their part, approximating, as it does, that of men, must be associated with the same continuous reproductive capacity that characterizes them.

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* Read before the Society, January 13, 1937.

Another factor that has operated to prevent a realization of what now appears to be the truth is the misunderstanding that has existed as to the biological analogies of human menstruation. In many animals the initiation of the mechanism producing ovulation, and the attendant phenomena of estrus, is indicated by slight vaginal bleeding; thus it seemed reasonable to conclude that menstruation stood in the same relation to human ovulation. Through study of the menstrual cycles of the other primates, however, this view of the matter has now been proved to be entirely erroneous. These studies have conclusively demonstrated that menstruation is an unique biological phenomenon, peculiar to man and the higher primates, and indicative, not of the beginning of estrus, but of the breakdown of the endometrial nest that, since the initiation of the preceding ovulation, has been undergoing an endocrine—controlled preparation for the reception of a fertile ovum. It is essentially, therefore, a process of de-nidation, tersely and in the main correctly interpreted by Powers in the dictum—"Women menstruate because they do not conceive." The correctness of this view is further demonstrated by the clinical observation that some women habitually experience some transitory, unilateral pain, possibly associated with slight vaginal bleeding—the Mittelschmertz and kleine Regel of the Germans—about mid-way between their periods; it is these phenomena that are biologically analogous to the bleeding preceding estrus in the lower animals, and not the menstrual bleeding of man and the other primates. A mid-month bleeding has also been observed to coincide with the initiation of estrus in some apes and monkeys. It is not to be wondered at, therefore, since modern science failed to solve the mystery of the relation of human ovulation and menstruation for so many decades, that the human mind, confronted with the phenomenon of continuous sexual activity in both sexes, failed, for countless ages, to grasp the fact, so essential in realizing humanity's consistent desire for sexual expression without reproductive consequence, that women can only conceive during a short but recurring period. And if it failed to attain this knowledge it certainly had to fail in any temporal orientation of this possibility to the menstrual cycle. It is this essential point that must now claim our attention.

In any living organism enjoying, if one may here use this word advisedly, bi-sexual reproduction, the spark of life is handed down from one generation to another by the union of the sperm cell, or male gamete, with the ovum, or female gamete, to form the zygote, the future development of which produces a new individual of the same species. When this takes place in the body of a female that retains the zygote during the process of its embryological development it is referred to as conception. The possible time or times, in relation to the menstrual cycle, when this occurrence is possible, will obviously depend upon the following factors:

1. The nature of the mechanism responsible for the production of ovulation.
2. The frequency and regularity or irregularity with which it functions.
3. The duration of the period, after its expulsion from the ovary, during which the ovum retains its ability to receive the spermatozoon.
4. The duration of the period, from the time of insemination, during which the spermatozoon retains its ability to enter and fertilize the ovum when subjected to the environment of the female genital tract.

These factors will now be considered.

It is unnecessary, for the purpose of the present discussion, to enter into any detailed consideration of the concatenation of endocrine events that constitutes the physiological mechanism controlling human ovulation, a mechanism shared by woman with all other mammalian females. Suffice it to say that under the influence of Prolan A, one of the gonadotropic hormones from the pituitary gland, the so-called "motor of the ovary," a growth of the graafian follicle is brought about; later the addition of the luteinizing hormone, Prolan B, from the same source, determines ovulation and the development of the corpus luteum, which in turn controls the preparation of the endometrium for the reception and nidation of a fertile egg. It is, however, of fundamental importance to our subject to know whether or not, in woman, the operation of this mechanism is subject to variations determined by sexual activity. It has been known for some time that in the cat, rabbit, and ferret orgasm is necessary for ovulation, and one can cite eminent medical authority, notably Grosser, claiming that orgasm may at least provoke ovulation in women. But the analogy with the animals mentioned is far from accurate. Proponents of this theory overlook the fact that, while copulation is necessary for the production of ovulation, in certain animals, these females copulate, with the possible exception of the rabbit, only at the period of estrus, when endocrine preparation for ovulation is already under way and the presence of the potent estrogenic hormone, estrin, impels them to seek sexual activity. This is an entirely different proposition from the assumption that human intercourse is capable of producing ovulation at any time, even when endocrine preparation for its occurrence has not been initiated or has already produced it. At the present time, therefore, its truth can be denied almost categorically. Dickinson and Beam have shown that women who fail to experience orgasm are as fertile as those who do, an observation confirmed by the consensus of medical opinion. But the evidence that appears most incontrovertible is furnished by the fact that in monkeys, animals whose sexual physiology is being increasingly shown to coincide exactly with that of man, ovulation is demonstrably never affected by either sexual activity or lack of it. Since this biological evidence has now been confirmed by a mass of clinical observations it seems safe to conclude that extra-ovulation invoked by orgasm is either impossible in women, or at least so rare an occurrence as to be negligible.

Since, then, it appears that ovulation in woman is entirely uninfluenced by any factors, sexual or otherwise, save those contributed by her interlocking chain of hormones, let us now attempt to sift the evidence available on the vital point of the physiological timing of this event with relation to her menstrual cycle. This evidence is derived from 3 different sources: first, there are the contributions from studies in comparative and experimental biology; second, those afforded by direct and objective clinical and laboratory observation; and, third, the subjective information furnished by women themselves. The time at our disposal will permit only a very cursory examination of these data.

Hartman, working with the rhesus monkey, has perfected a technic for determining the occurrence of ovulation by combined recto-abdominal palpation of the ovary. Counting from the first day of the last mentrual period he found the following distribution of ovulation in 108 observations: eighth day, 2; ninth, 5; tenth, 9; eleventh, 16; twelfth, 17; thirteenth, 22; fourteenth, 16; fifteenth, 8; sixteenth, 9; seventeenth, 2; and eighteenth and twentieth, 1 each. In no instance was ovulation observed on any other days in the cycle and approximately two thirds occurred on the eleventh to fourteenth days, inclusive. These findings have been confirmed and checked by recovery of eggs from the tubes and by observations on the ages of embryos and the development of the corpus luteum. Similar but much less extensive data point to the same timing of ovulation in the baboon, the Java macaque and even in the chimpanzee. Hartman says: "I have looked hundreds of times for signs of ovulation within the last week or 10 days of the cycle. I have never found it and don't expect to. The physiology of the menstruating female precludes the probability." From all of this evidence it may be accepted that ovulation in the sub-human primates takes place within the range of a very few days around the middle of the menstrual cycle.

Since woman must be biologically classified as a primate, it is not surprising to find that the available clinical and laboratory evidence points clearly to the same mid-cycle timing of her ovulations. Without here attempting details, the character and sources of these confirmatory data may be summarized as follows:

1. Quantitative assays of the hormone levels in blood and urine.
2. Cyclical changes in the endometrium demonstrated by biopsy of endometrial scrapings.
3. The time of abolition of uterine response to stimulation with pituitrin due to the inhibitory action of the corpus luteum.
4. Timing of ovulation and corpus luteum formation as determined by direct inspection of the ovaries at laparotomies.
5. Recovery of the human egg from washings of the fallopian tubes.
6. Demonstration of cyclical changes in the vaginal epithelium in women corresponding to those observed in animals, and characterized by the same copulatory phase just before mid-cycle.
7. The ages of early human embryos as determined by Hartman by comparison with monkey embryos of known age.
8. The greater success of artificial insemination when practiced around the mid-cycle period.

This experimental and clinical evidence is corroborated to a certain extent by subjective evidence furnished by women themselves. Whether for or against our thesis, most of this must necessarily be taken *cum grano salis;* as one distinguished student of the subject, best left nameless here for obvious reasons, was once heard to remark—"Monkeys can be kept under lock and key, but women are the biggest liars in the world." Nevertheless, the evidence is suggestive. The curve of sex-desire in women has never been satisfactorily determined and conflicting values are obtained for it by different students and different methods. That of Marie Stopes shows exacerbations at the mid-month and just before menstruation. Most of my own patients place the maximum of desire in the postmenstrual period and its lowest ebb in the last half of their cycles. But a few women tell me they are most passionate during pregnancy; such cases demonstrate that the psychological element of freedom from worry about conception is not only fairly obvious, but one admitted to be controlling, and show that all such data must be accepted with extreme caution. The reputation of orthodox Jewish women for fertility is interesting and pertinent when it is realized that, according to the Mosaic law, they must refrain from intercourse for a period of 7 days after the end of menstruation. This approximately 12-day period returns them to their husbands' arms at what we now believe to be the optimum time for conception. The occasional occurrence of intermenstrual pain and bleeding evidencing ovulation has already been noted. Without adequate contraception the great majority of women who marry in the latter half of a menstrual cycle menstruate once after marriage, while those marrying in the first half seldom do. My own clinical records certainly confirm this observation. Inaccurate and unreliable as undoubtedly is the evidence based on conception following a single coitus, or on the German and Italian statistics covering soldiers' furloughs at home in relation to their wives' cycles, curves based on such data uniformly show the peak at the mid-month period, while, at the same time, it must be admitted, indicating the possibility of conception at any time. It is the questionable reliability of such data, of course, that has called forth the humorous comments noted above.

With an accumulation of evidence of such different sorts and from so many different sources it seems reasonable to accept it as proven that the great majority of women ovulate within a range of a few days about the middle of their menstrual cycles; it remains to be seen if there are methods now available for a closer approximation of this vitally important date. The observations of Ogino, and Knaus, made entirely independently in Japan and Austria, throw additional light on this point and are relied upon by all of the numerous authors of the books and articles that exploit the whole "safe period" theory for the laity. Ogino, basing his conclusions on a very large amount of clinical study of the dates of fertile and sterile intercourse and of the condition of the follicles or corpora lutei observed during the course of laparotomies, has determined to his own satisfaction that in 542 out of 557 cases ovulation occurred from the twelfth to the sixteenth day before the onset of the menstrual period. Knaus, making an experimental approach to the problem, places its occurrence from the fourteenth to the sixteenth day before the period. He studied the reaction of the human uterus to stimulation with pituitrin at different times in the cycle and found that in woman, as in the rabbit, its response was inhibited by the activity of the corpus luteum, the presence of which naturally afforded indubitable evidence of the occurrence of ovulation. It will be seen that these two authorities agree in relating the time of ovulation to the approaching rather than the past menstrual period. Their findings would indicate that in cases of menstrual irregularity it is the duration of the resting phase of the endometrium that is variable, but that the active, luteal phase has a constant mean value of approximately 14 days, determined by the life cycle of the corpus luteum of ovulation. In other words, the woman menstruating regularly on a 28-day cycle ovulates 14 days before and after the onset of her periods; on a 35-day cycle ovulation occurs on the twenty-first day after the onset; and in cases of marked irregularity, with periods of amenorrhea, the date of the next period will be 14 days after ovulation finally occurs. It must be admitted that Hartman has found no evidence of such a relationship in the rhesus monkey, in which the time of ovulation appears to be independent of the length of the menstrual cycles, and this fact alone would make unqualified acceptance of Ogino's and Knaus' work premature at this time. At best it is readily seen that the dating of ovulation by practical application of this knowledge, even if true, will depend entirely on the ability to accurately date the approaching menstrual period.

It would certainly be rash, however, to hold that the future, and possibly the very near future, will not witness the determination of a method or methods for exactly timing ovulation. Further confirmation of Knaus' method of manometric observation of uterine response to pituitrin is very possible. Or an approach to the problem through more refined methods for quantitatively assaying the hormones concerned may be perfected. Very recently Burr, Hill and Allen have discovered that ovulation in the rabbit sets up changes in electrical potential in the pelvis that are not only detectable but susceptible of observation through application of the principles of the electrocardiograph. By their method, believed to be applicable to women, these investigators have even been able to count the number of follicles that rupture. Should these eventualities come to pass it will require a seer to cast the horoscope of the epoch of social, economic and moral change upon the threshold of which humanity now stands. But it takes no prophetic vision to foretell the startling effect on the practice of medicine! My own experience leads me to believe that a very large proportion of Aschheim-Zondek tests are preliminary to criminal abortion; this business the laboratory clinician will lose. But in his ability to exactly time ovulation he will gain a compensatory and tangible asset that will be to him what the appendix is to the surgeon, or even, not to stretch the analogy to the bursting point, what the tonsil is to the otolaryngologist.

To make such present or future knowledge applicable to the control or promotion of fertility it is obvious that only two additional factors in the equation of conception must be determinable, namely, the life expectancy of the unfertilized ovum, on the one hand, and of the spermatozoa in the environment of the tube, on the other. Knowledge on these two points is largely based on empirical data derived from clinical observations on the reproductive results of cohabitation at different times in the menstrual cycle, and on biological analogies determined from breeding experiments with monkeys and other laboratory animals. These data are furnishing evidence that both the egg and the sperm have a very short life expectancy in the face of any factors preventing their union. For the human ovum this period is believed to be less than 24 hours. This unexpectedly short life span has been determined on because, first, the few successful attempts to recover the human egg from the fallopian tube have been made exactly at the estimated time of ovulation; second, a large series of reported cohabitations at very short intervals following the estimated date of ovulation have remained infertile; and, third, of analogies based on the accurate determination of the duration of the period of fecundability of the ova of monkeys and guinea-pigs. Hartman has found that while female monkeys kept in isolation from the males during the early stages of estrus but released to them immediately after rupture of the follicle copulate immediately and repeatedly, they consistently fail to conceive. There was only one exception noted, in which intercourse 18 hours after ovulation was fertile. The significance of these findings is rendered even more conclusive by the work of Young and Blandau. These observers have shown that the egg of the guinea-pig can be fertilized for 12 hours after its extrusion, and that the resulting embryos are normal. In the following 6 hours fertilization occurs less and less frequently and results in a larger and larger proportion of abnormal embryos, and in the few cases of fertilization occurring after 18 hours the resulting embryos all die. Since all of this work is confirmed by veterinary experience in the breeding of domestic animals, it now appears that, in the absence of fertilization, the life span of the mammalian egg, including that of man, is a matter of a few hours only.

By analogy it would seem reasonable to believe that what holds for the egg must also hold for the sperm. In opposition to such a view, however, notice must be taken of the many reports in the literature of the recovery of motile human spermatozoa from the uterus, and even from the vagina, at varying intervals up to many days after the admitted date of the last insemination. Without disputing the veracity of the women on whose statements such reports depend for their validity, it now seems necessary to conclude that motility of the sperm persists for a longer period than does its ability to penetrate and fertilize an ovum, and, therefore, that motility is no index of the retention of its capacity to fecundate. This opinion is backed by an increasing accumulation of supporting facts. Thus, it has been found that in animals, of whom man is one, in which the testicles are contained in a scrotum, exposure of the sperm to the higher internal temperature of the female body rapidly results in the loss of their fecundating power. Hammond and Asdell have certainly proved this for the rabbit. By ligation between the head and tail of the epididymis these observers demonstrated that, in the male genital tract, the sperm remained motile for over 2 months and retained fertility for as long as 40 days. They then performed a most ingenuous series of experiments, by availing themselves of the fact that in the doe rabbit ovulation follows orgasm in 10 hours. Does were carefully artificially inseminated and then, after varying periods of time, subsequently bred to vasectomized males in order to produce the orgasm necessary to insure ovulation 10 hours later. Thus by adding 10 hours to the time elapsing between artificial insemination and sterile copulation they were enabled to determine the fertility of the sperm after various intervals of time. They found that conception never occurred where this interval was greater than 30 hours. This proved that, in the rabbit, spermatozoa that retain fertility for 40 days, when stored in the male, lose it in 30 hours or less in the tubes of the female. The application of these facts to man is rendered extremely likely by the results obtained by clinical study of series of cases in which intercourse more than 3 or 4 days before ovulation has proven to be consistently infertile and by the result of breeding experiments in monkeys, where the various factors involved are susceptible of exact control.

The acceptance of this physiological picture as accurately portraying the sequence and timing of the events of human conception imposes on the physician the duty of familiarizing himself with the methods devised for its application to certain practical medical problems. Certainly the great majority of women are incapable of subjectively even approximating the exact time of ovulation, which is obviously the essential factor. Until this can be done by them, or for them, by appropriate laboratory tests that may yet be devised, this vital date must be estimated by the physician. In doing this, in the present state of our knowledge, it seems safer to allow 2 days before and after the theoretical date of ovulation. This results in placing its occurrence somewhere in a 5-day period covering, inclusively, the twelfth to the sixteenth day before the beginning of the next menstruation. To these 5 days it is necessary to add 2 days before the twelfth, to cover the term of functional activity of the sperm, and 1 day after the sixteenth, to allow for the death of the egg. The resulting inclusive period of 8 days, from the tenth to the seventeenth day before the expected date of menstruation, is thus determined upon as the period of possible fertility. It will be observed, however, that these dates refer to days before the onset of the next menstruation, and the accurate determination of this date, while of the utmost importance, will be easy or difficult depending upon the regularity of the menstrual cycle in any given patient.

This point is of such vital moment that it merits particular consideration. Many statistical studies of menstrual regularity have been made, the resulting estimates of regularity ranging from 70 per cent to 90 per cent of all cases. Novak states that 4 women out of 5 menstruate at 28-day intervals, with variations of only a day or 2 each way. If the so-called method of rhythm is to be successfully applied to the prevention of conception, it becomes necessary, however, to pay close attention to the question of irregularity. My own experience is that women tend to overestimate their degree of regularity. They will state that they are regular when a subsequent check, by keeping an accurate record, will disclose very significant variations. Thus, in the case of 1 patient, who was anxious to control conception by this method, and who stated that she menstruated regularly every 28 days, with a variation of only a day or 2 either way, records carefully kept over a period of 19 months resulted as follows: 25-day cycle, 1; 26-day, 3; 27-day, 5; 28-day, 3; 29-day, 2; 30-day, 2; 32-day, 2; and 33-day, 1. It is advisable, therefore, to have an actual calendar record covering a period of at least a year, before estimating a patient's periods of fertility and sterility, and, in the absence of such record, to make ample allowance for all possible irregularity. Known irregularity is allowed for as follows: the difference, in days, between the shortest and longest cycle is added to the 8 days allowed for the duration of the fertile period when there is absolute regularity. The duration of the fertile period in any given patient is then determined by adding the total number of days of possible irregularity to the figure 8.

Let us now observe the practical application of this rule to an actual case. Assume a patient to vary between 26 and 30 days; actually few will be found more regular than this. Taking the shortest cycle of 26 days we estimate the theoretical date of ovulation 14 days previously, or on the twelfth day after the last period began. Four additional days before this date must be allowed, 2 for possible earlier occurrence of ovulation and 2 to cover the span of fecundability of the sperm; this calculation places the first day of the possible fertile period on the eighth day after menstruation began. If the patient were regular with a 26-day cycle this day, the eighth, would be the first of a fertile period of 8 days, made up of the 4 days previous to the theoretical day of ovulation, the day of ovulation itself, 2 days after this to allow for late ovulation, and 1 additional day to allow for death of the egg; since she is irregular, however, her cycles varying between 26 and 30 days, we determine the extent of her possible irregularity by subtracting the figure representing her shortest cycle from that representing her longest. The figures being 26 and 30, respectively, the difference is 4, and this figure is now added to 8, to make a total of 12, the number of days of the possible fertile period in this particular patient. She may then be advised to consider the day on which she begins to menstruate as the first day of her cycle and, counting from this date, that her fertile period extends from the eighth to the nineteenth day, inclusive. Authors of books intended for lay readers uniformly express this rhythm of fertility and sterility for their readers by demarcating a first and second sterile period in each cycle, separated by the mid-month period of fertility. However, the practical application of this method is susceptible of simplification both for the patient and physician. Taking the case just studied, of a 26- to 30-day cycle, we have seen that the eighth day is the first day of fertility; the seventh day is then the last day of the first sterile period, and this date may be determined in any type of cycle by adding 1 to the second digit of the number representing the shortest cycle if it be 29 days or less, and 11 if it be 30 to 39: 26, second digit 6, add 1, equals 7. To this figure we now add the sum obtained by adding to 8, the length of the fertile period in a regular cycle, the total days of possible menstrual irregularity obtained by subtracting the number of days in the shortest from the number in the longest cycle. In the case cited this is 4, which, plus 8, gives 12; 12 added to 7 gives 19, indicating that the nineteenth day is the last day of possible fertility. On these established facts the patient is advised as follows: "Counting the first day of your menstrual period as 1, you are sterile beginning on the twentieth day and remain so up to and including the seventh day after the beginning of your next menstrual period."

Such advice from a physician to his patient may be practically applied by her to the attainment of two diametrically opposed ends, namely, either the promotion or prevention of conception. Its successful employment in either way by a sufficiently large group of women would certainly afford important corroborative clinical support for the soundness of the physiological facts on which it was predicated. Accumulating clinical experience is doing just this. With respect to the promotion of conception Kurzrok has recently reported cases of sterility in orthodox Jewesses with short menstrual cycles cured by advising intercourse earlier in the cycle than allowed by strict Mosaic law. Such sterility is readily explained by the fact that continence for 7 days following a 5-day menstrual period in any woman with a cycle of 24 days or less would limit all intercourse to the sterile period. Appropriate advice regarding the fertile period has enabled Albrecht to secure pregnancies in 26 out of 65 patients who had been sterile for from 2 to 6 years. Several such cases have been observed in my own practice, the most striking of which was as follows: I was consulted by a young woman regarding sterility of 8 years' duration. Ordinary examination disclosed no pelvic pathology or evidence of endocrine imbalance. The anamnesis disclosed no relevant disease in husband or wife but did elicit the fact that this couple were unusually abstemious regarding intercourse, partially because of some aversion to it on the part of the wife and partially because the husband's business required considerable absence from home. Her fertile period was determined by a careful analysis of her menstrual cycle, and she was advised to try having intercourse every other night during it, for a period of 2 or 3 months, before submitting to any more detailed study of her situation. She was in the second sterile phase of her cycle at the time she consulted me, but menstruated only once after receiving this advice; she was delivered of a healthy male infant at term. The practical importance of bearing such facts as these in mind in timing any attempt to secure pregnancy by artificial insemination is too obvious to require comment.

Naturally, however, it is the application of knowledge concerning the fertile period to the control of conception, rather than to its promotion, that has aroused the most widespread interest. Several books and many magazine articles on this subject, laying down rules through the use of which any reasonably intelligent woman may determine her own fertile period, have enjoyed a very large and entirely unrestricted circulation among the laity, with the result that a very considerable clinical test of periodic continence as a means for attaining contraception has been had. While some failures have been reported it cannot be denied that the evidence adduced from this popular trial is decidedly on the side of success for this method and hence corroborative of the soundness of the theory on which it is based. The most widely read book is "The Rhythm," published by the Latz Foundation, which also has sold over 80,000 so-called "Concip Calendars," a device to facilitate determination of the fertile and sterile phases of the menstrual cycle. The statement of Latz that "It may be reasonably assumed that if the rhythm theory were devoid of all value, the offices of the Latz Foundation would have been deluged with complaints from disappointed purchasers of the book, from their physicians, from clergymen, etc."—may certainly be accepted, to put it mildly, as unexaggerated. Yet he further adds that, "About 20 complaints have been received that the rhythm theory 'did not work'." In a recent article Miller reports over 2,200 acts of intercourse during the sterile phase of the cycle in a group of 154 couples without a single resulting pregnancy, and these results are similar to others reported in medical literature. Taken altogether, the evidence available suggests only entire agreement with the statement of Latz that "We can confidently say that upwards of 50,000 cohabitations, during most varied menstrual cycles, and under the greatest variety of circumstances, is evidence of the reliability of the rhythm theory."

If, then, we accept all this accumulation of evidence as establishing the practicability of securing birth control by practicing intelligent periodic continence, to what place must we assign this method in the armamentarium of the practicing physician? In order to answer this question it is necessary to evaluate its intrinsic merits and faults. Possibly it would be unnecessary to do this were it not for the fact that many of its proponents claim it to be so certain, so susceptible of universally successful application, that it renders all methods of mechanical and chemical contraception unnecessary. This bald statement was recently made by a distinguished professor of obstetrics at a hearing on birth control before a committee of the Congress. At the present time the truth of this assertion can be categorically denied; and even if the future should witness the development of a practical method or methods for exactly determining the onset and duration of the actual period of fertility, which, as we have seen, probably does not much exceed 48 hours in length, it will still fall short of entire truth. For these reasons it is now proposed to examine this so-called "natural" method of birth control from two points of view: first, in the light of the difficulties that arise in attempting its practical application to some every-day problems of medical practice, and, second, in the light of certain biological generalizations concerning normal human sexuality.

We have already seen that the estimation of the "safe period" is based on the assumption that ovulation occurs at a reasonably fixed interval before the next ensuing and not after the last menstrual period, the inevitable result being that its demarcation will be easy or difficult in proportion to the regularity of the cycle. It is unnecessary to enter into any detailed statistical study of menstrual irregularity; every physician knows it is very common. Since even in a regular cycle the theoretical fertile period must be estimated at 8 days, to which must be added every day of possible irregularity, it follows a variation of only 5 days, which may be accepted as average, entails the observance of a fertile period of 13 days. If to this sum we add the days of menstruation, say 5 in number, believed by most patients to be unavailable for intercourse anyway, we observe that the woman practicing this form of birth control is incapacitated for her marital relations for 18 days in each menstrual cycle. Put in another way, this woman must observe continence for about 234 days in each year as against 65 days necessary for her sister who is using adequate modern contraceptive measures.

At best, then, it should be obvious that this method is available only for the educated few, who constantly exercise a restraint in sexual matters all too rare in any stratum of society. How practicable is such a procedure likely to be in the tenement district of a large city? Yet it is these women and their children who themselves not only suffer most from the evil effects of uncontrolled childbearing, but whose proclivities add the greatest burden to the already groaning tax-payer. But what of the woman whose irregularity much exceeds the limits just mentioned, or of the one who has no regularity at all? For them this method is not merely impractical; it is entirely unworkable. Are they not entitled to help in their problem if medical science can afford them an answer? Finally, what of venereal prophylaxis? Certainly periodic continence is no answer to this problem and holds out no hope to the conscientious physician forced to advise an appropriate marriage hygiene in the face of syphilitic infection.

But, serious as these disadvantages are, there are others of equal or even greater moment to claim our attention. These center around this simple question: Is it desirable that spontaneity of sexual expression in marriage should be chained to a calendar,or that the tides of normal desire should be forced into conformity with a time-table? An intelligent answer to this question necessitates what may at first appear to be an irrelevant digression.

All life is endowed with three primitive concerns that may be alliteratively summed up as sex, sustenance, and security; in this trilogy, sex, since it has to do with the perpetuation of all life, is inevitably paramount; the other two are secondary. All the evidence of anthropology, and even that of history as well,demonstrates that man has never escaped this primordial, trinitarian inheritance, that modern man lives under its compulsion as surely as did the ape-jawed Piltdown man or the ape-man of Java, hundreds of thousands if not millions of years ago. Furthermore, no matter how religion, ancient or modern, may have, as Shakespeare said, these truths "sicklied o'er with the pale cast of thought," and so succeeded in directing the human intellect to speculation concerning a future rather than a present existence, man, as a biological unit, has ever continued to function physiologically along lines laid down by his physical evolution. Once this evolution of man from lower mammalian forms be accepted, and no scientific opinion can be found to gainsay it, one must also, of necessity, accept sex as one of the most important controlling factors not only in directing its course but in determining its goal, the intellectual supremacy of man over all animate creation. And it is peculiarly interesting to realize that sex has thus affected man's destiny, even after he was man, as a blindly operating force, an unthinking urge, unconnected in either brute or human psychology with its reproductive consequence. There are savage tribes alive today that have failed to solve the riddle of reproduction, that see no connection between their sexual activities and childbirth. In the last moment of time, comparatively, civilized man has solved this age-old problem; is it likely, or even desirable, that his new intellectual approach to the mystery of sex should, in the twinkling of an eye, release him from its thraldom? Is it not more likely, more desirable, that in the future as in the past it should continue to light the way that leads to his unknown destiny?

Since these truths are fundamental in applying human knowledge to the problem of birth control, now happily admitted by all to be not only desirable, but inevitable if man is to finally release himself from the more cruel manifestations of the law of survival of the fittest, let us glance momentarily at human sexuality in the light thrown on it by comparative biology. We have seen that the pattern of sexual behavior among the primates, man, apes, baboons, and monkeys, is *sui generis*, unique among all other mammals in the constant favorable response of the females to the copulatory advances of the males, an acquiescence that is present at all phases of the estrus cycle and even during pregnancy. When Swift, in "Gulliver's Travels," wrote of his caricature on humanity, the Yahoo, that "the she Yahoo would admit the male while she was pregnant" he demonstrated his complete ignorance of simian biology, pardonable, however, since he did not have available over 200 years ago the modern monographs of Bingham, Hartman, Miller, Yerkes, and Zuckerman. The work of these observers has shown all too clearly that man shares his sexual behavior with his simian cousins to such an extent that every possible variation in what we are pleased to call normal and abnormal sexual conduct in man, including prostitution but excluding rape and monogamy, is foreshadowed among the lower primates. All of this goes to show that man's perennial interest in sex is not only bred in him, so to speak, but has largely contributed to placing him where he is. As he crept up from the night of the brute toward the dawn of humanity, sex has encouraged a communal existence and made isolation impossible, thus stimulating intelligence in the fight for survival; it has made possible the prolongation of gestation and infancy, thus sowing early the seeds of altruism and affection; it has stimulated the development of that rarest of biological phenomena the impulse to mate instead of merely to copulate, thus laying the foundation for the essential unit of modern society, the family; it has tinctured his religion and dominated his art, largely colored his literature and usurped his poetry; it has filled his asylums and, with venereal disease, killed without mercy; it is something no physician, to be worthy of his title, can ever once afford to forget. In a word, it still remains the mainspring of life.

The studies of the sex lives of the lower primates have furnished another important analogy, most pertinent to our subject. In his recent provocative work on "The Science of Human Reproduction," Parshley says: "In all the primates—as opposed to lower mammals—sex behavior is freed from rigid endocrine control . . . and therefore, the way is open for all sorts of personal and social stimuli to become effective and for sexual phenomena to play a large part in life aside from the strictly reproductive function. Such an extension of the sexual element can hardly be regarded as unnatural in man, when it is found to be a typical primate characteristic." This is a very admirable summary, but it is to be noted that he employs the term—"freed from rigid endocrine control." This can only mean that the release has not been complete or perfect, and all the observers agree that, for the lower primates at least, this is undoubtedly true. Since the primates were evolved from lower mammalian forms in which sex was, and remains, under "rigid endocrine control," it is not surprising to find that the sexual conduct of simian females becomes more and more aggressive as the time of ovulation approaches; the endocrines no longer dominate but they still play their part. At the copulatory phase of the cycle the female is also obviously more attractive to and more sought out by the males, and her response now loses a certain behavior pattern that, at other phases of her cycle, suggests a condition reflex strongly foreshadowing the basic factors underlying human prostitution. These facts, admitted by all students of this subject, point a lesson for those studying human sexuality. It seems reasonable to believe that sexuality in women has been even more emancipated from endocrine control than in female apes and monkeys; music, drama, art, and literature provide them with new sexual stimuli unknown to the brute and, as Hartman writes—"The monkey husband doesn't bring gifts, take his wife to the seashore, nor throw gay parties." Nevertheless it seems equally reasonable to believe that women have not completely escaped the control of their endocrines, and that the flood tide of their desire must still coincide with ovulation time and its ebb with the "safe period." This is certainly sound biology and physiology, well understood by physicians who lend a sympathetic ear to the sexual problems of their women patients. The physician approached for advice by the husband practicing periodic continence as a means of contraception may, therefore, appropriately call his attention not only to the humorous statement of Hartman, quoted above, but also to one of Balzac's, who said that in making love to a girl the performance of the average man was much like that of an orang-outang with a violin. In both instances, if the result be cacophony rather than harmony, it seems safer to blame the skill of the performer rather than the responsive qualities of the instrument.

It is on such sound physiological grounds as these that we give a negative answer to our question regarding the applicability of the calendar and time-table to human sexuality. Birth control is an essential and vital component of modern marriage, not alone on the medical grounds of preserving life and health of mothers and babies, but for sound economic reasons, and, in the matter of preventing war, for even sounder reasons of world policy. But modern marriage is in a state of flux, the object of attack from many sources. Grant that in its monogamous form it is the perfect formula for sexual expression, idealize it as one pleases, compare it, as has been done, to a gorgeous rose bush in full bloom; the fact remains that, like the rose bush which must be rooted in rich soil, it languishes and dies unless its tendrils dig deeply into the primordial depths of sexual desire. After all, this is of its essence. If, then, birth control is to protect and promote marriage, if it is to be a constructive and not a destructive factor in finding the correct answer to the modern sex question, it must always function in accordance with, and not oppose, sound biological principles. As Havelock Ellis points out, all concerned in this problem may well keep in mind the infinitely wise words of Shakespeare: "Love talks with better knowledge and knowledge with dearer love."

In conclusion, how can we finally estimate the value of the "safe period"? After my own experience with and study of it I can only cite the following impressions:

1. It is more susceptible than any other method to perversion to the promotion of promiscuity and immorality.
2. When determined by a competent physician or intelligent layman on reliable menstrual data, it is believed to be as reliable as any other known method of contraception.
3. Since it is impractical for a considerable proportion of women, and unworkable for some, it is in no sense a uniformly satisfactory method.
4. It tends to destroy spontaneity in marriage because it savors too much of punching a time clock.
5. To the extent that it forces intercourse contrary to the normal, physiological tides of desire, it is anti-social and will tend to destroy rather than promote marriage.
6. It will never be an answer to the necessity for certain and positive venereal prophylaxis.
7. Therefore, until such time as its limits can be much narrowed and its exact timing more accurately determined, it can legitimately only be considered as a method accessory and complimentary to ordinary methods of contraception.
8. Used in this way, and for the prevention or cure of sterility, it is a very valuable and practical addition to medical knowledge.

And, finally, another quotation from Havelock Ellis: "There is no field in which it is more necessary than in that now before us for the physician to acquire a wider knowledge or to exercise a finer intelligence."

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ARTERIOSCLEROSIS

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Arteriosclerosis is a chronic disturbance of the vessels which manifests itself by deposits of the most varied kinds in the vascular walls and becomes irreversible on attaining its climax in vessels impaired by changes incident to the process of aging, with consequent deformation of the lumen and brittleness of the vascular walls.

Although our definite knowledge of this condition is still comparatively meager, nevertheless it represents the accumulation of several centuries. Written descriptions of arteriosclerosis in man appear first in the works of the anatomists who followed Vesalius. In the eighteenth century Vieussens, Crell, von Haller, Boerhaave, Morgagni, and Scarpa contributed the original theories of its pathogenesis. The French, English, and Viennese schools of the early nineteenth century made numerous valuable clinical observations on arteriosclerosis, but their descriptions of the pathology were either incomplete or inaccurate. For example, Rokitansky stated that the intimal lesions in arteriosclerosis were a surface deposit from the blood stream. It remained for Virchow to lay the basis for our modern conception of blood-vessel pathology.

An important contribution was made in 1872 when arteriosclerosis was first accurately described by Gull and Sutton. Arteriosclerosis was differentiated from syphilitic arteritis by Huebner, Welch, and Döhle toward the close of the nineteenth century. During the present century new theories concerning the pathogenesis of arteriosclerosis have been proposed by Thoma, Jores, Marchand, and Klotz, and studies of the relation of hypertension to arteriosclerosis made by von Basch, Mahomed, Allbutt, and Huchard.

Microscopic sections of the aorta and other arteries of well-preserved Egyptian mummies have revealed unmistakable evidence of typical advanced arteriosclerosis. So it is obviously an ancient disease and not one that can be attributed merely to the rapid pace of modern civilization. However, although its history goes back to the dawn of mankind, the study of arteriosclerosis was strangely neglected until comparatively recent times. No doubt this was due to the belief that it was a natural process which was beyond all human control. It was not until lesions resembling arteriosclerosis were produced in animals by experimental methods that real interest in the subject was stimulated. Furthermore, the observation that many persons live to extreme old age without exhibiting serious deterioration of their arteries, while severe sclerosis is sometimes found in young persons, awakened the suspicion that the environment might play an important rôle and roused the hope that a more accurate understanding of the etiologic factors involved might enable us to control the disease.

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MORBID ANATOMY

Most authors now accept the division of arteriosclerosis into 3 groups:

1. Atherosclerosis.
2. Medial (or Mönckeberg's) sclerosis.
3. Hyperplastic or arteriosclerosis.

1. Atherosclerosis occurs in its most typical form in the abdominal aorta and the iliac arteries. It is also found commonly in the coronary and cerebral arteries. The initial changes are in the depth of the intima where we find an infiltration of lipoid material. This is associated with the proliferation of fibrous tissue in the superficial layer of the intima, with the resultant production of grayish yellow plaques that project above the inner surface of the vessels. The material in the depths of the lesion undergoes necrosis and forms a mushy, gruel-like mass, the so-called "atheromatous abscess." The necrosis may be quite extensive and involve even the superficial layers of the media. From this point on, further change may take place in 2 directions, i.e., either the surface is permanently sealed by the development of a calcareous plate, or the degenerative changes extend through the fibrous covering to the surface and the atheromatous masses are partly washed away by the blood stream, leaving ragged ulcerations. These may be partly or completely covered with thrombi. Hyaline streaks in the media and slight perivascular round-cell infiltration of the vasa vasorum have also been noted by some histologists. Recently, Wolkoff in her studies on coronary artery disease has confirmed the earlier observation of Jores that splitting of the internal elastic lamina is a constant finding in atherosclerosis.

2. Mönckeberg's sclerosis is most common in the muscular arteries, particularly those of the lower extremities. It consists of a primary necrosis and calcification of the media which is not necessarily associated with intimal lesions. The calcareous deposits may be plate-like, circular, or continuous over long stretches of the arteries. It is interesting to note at this point that the vascular lesions which have been produced in animals by the injection of epinephrine, irradiated ergosterol, and numerous other substances resemble this type of sclerosis rather than atherosclerosis.

3. Hyperplastic sclerosis is found in the arterioles and small arteries (most commonly in the kidney, less frequently in the spleen and pancreas). It is characterized by endothelial proliferation followed by an accumulation of hyaline material. The process may go on to complete closure of the lumen. An hypertrophy of the muscular wall is sometimes associated with the intimal lesions (due probably to the high blood pressure which is frequently associated with hyperplastic sclerosis).

ETIOLOGY

Aschoff, one of the pioneers in this field, says: "In scarcely any other disease do so many factors coöperate in its origin as in arteriosclerosis." Let us examine these factors. First, there is hypertension. This has long been recognized as an important cause of arteriosclerosis, particularly the diffuse hyperplastic type involving the small arterioles (as shown by the studies of Jores, Fahr, Evans, and Fishberg). Furthermore, Kernohan, Anderson and Keith have actually succeeded in demonstrating hyperplastic changes in the arterioles of patients with hypertension by means of biopsy material removed from the pectoralis muscle. Lange points out that there are cases of pure arteriosclerosis and pure hypertension, but even he admits that in the great majority of instances hypertension leads to sclerosis, as demonstrated by the roentgen ray, with cerebral and renal changes.

The increased pressure, it is believed, causes greater wear and tear of the arterial wall and thus hastens the sclerotic process. The importance of injury to the media by stretching of the elastic tissue has been emphasized by Thoma and Klotz and also by Wells in his theory of aging colloids. Lange has offered an explanation which differs somewhat from this mechanical pressure theory. He has shown that the most constant peculiarity of hypertonic blood vessels is that they are unusually responsive to stimulation. It follows that hypertonic arteries are subjected by physiologic stimuli of human life to greater and more continuous alterations in their width than normal arteries. The increase in dilatations and contractions of the arteries represents a permanent increase in the work performed and a greater wear and tear (the latter term being interpreted not in a purely mechanical sense, but taking into account the changed nutrition of the arterial wall, together with functional disturbances in the vasa vasorum and in the arteries themselves).

A second factor is heredity. Aside from the fact that it is quite natural to suppose that different persons are endowed with vascular tubing of different quality and durability, there is other evidence which implicates heredity. Numerous instances are recorded in which several members of a family or several generations exhibited nephritis, or cerebral or myocardial evidence of arteriosclerosis. For example, Hurst tells of a case in which 16 members of a family of 27 suffered from nephritis. Studies of identical twins have also produced confirmatory evidence.

To Anitschkow, the Russian histologist, belongs the credit for focusing attention on the importance of cholesterol metabolism in arteriosclerosis. By feeding rabbits pure cholesterol dissolved in vegetable oil, he was able to produce lesions in the aorta which closely resembled human atherosclerosis. He further showed that removal of the testis or thyroid facilitated experimental arteriosclerosis, which indicated that the endocrines play some part. He found also that if local lesions of the arterial wall (which may be produced by such substances as viosterol, epinephrine, or thyroxin) are combined with cholesterol feeding, atherosclerotic changes will develop in those places where the lesions are situated, provided hypercholesteremia is present. Anitschkow summarizes his results on experimental atherosclerosis as follows: (1) The lipoidal accumulations in the arteries represent an infiltration of the latter with lipoids circulating in the blood; (2) all subsequent hyperplastic processes are to be regarded as a reaction to the primary deposition of lipoids; (3) cholesterol plays the principal part in this deposition of lipoids in the arterial wall. Anitschkow admits that other factors (mechanical, toxic, infectious, and nervous) may act as predisposing causes, but thinks the disturbance in cholesterol metabolism is the exciting factor. Leary, in defending Anitschkow's views, calls attention to the fact that the use of a high fat diet by human beings in the treatment of diabetes in the decade from 1920 to 1930 resulted in a marked increase of arteriosclerosis even in children. He quotes Warren as stating in 1930: "I have yet to see at autopsy a diabetic or to read of the autopsy of a diabetic, whose disease has lasted 5 years or more, who was free from arteriosclerosis, regardless of age . . . the diabetic has not only more than his share of arteriosclerosis, but it falls to his lot 10 or 12 years earlier than to the non-diabetic." Joslin, and Rabinowitch have actually reported a decrease in incidence of arteriosclerosis since the use of the low fat diet.

Duff, of Johns Hopkins University, has recently subjected the work of Anitschkow to drastic criticism. In addition to some anatomic discrepancies in the lesions of man and rabbits, he points out very distinct differences in the cholesterol metabolism of man and rabbits, and cautions against applying results in the latter too closely to human atherosclerosis. He asserts that the frequent association of diabetes and arteriosclerosis is probably due to hyperglycemia, ketosis, or commonly occurring infections, rather than to hypercholesteremia. In support of this view, he refers to the fact that in other conditions in which hypercholesteremia is present, such as pregnancy, hypothyroidism, and obstructive jaundice, there is no increased incidence of arteriosclerosis. Duff believes that human arteriosclerosis is initiated by some arterial injury whose cause is still obscure. The lipoids are deposited secondarily, inasmuch as they do not accumulate diffusely everywhere in the wall, but in localized and restricted areas. If the original injury which initiated the whole process ceases to operate, it is probable that the lipoid deposits prevent immediate healing and continue to exert their influence, so that the lesions persist and progress slowly.

In justice to Anitschkow and his theory, it may be said that Duff has not eliminated the possibility that a disturbance in cholesterol metabolism may in itself be sufficient (by virtue of the deposition of lipoids) to produce the primary arterial injury whose cause is still shrouded in mystery. Further studies on the biochemistry of cholesterol may help to solve this problem.

Dietary disturbances (other than those from cholesterol) are now regarded as possessing little influence upon the development of arteriosclerosis in otherwise normal individuals. However, Minot and Weiss emphasize the point that a suboptimal diet over a long period of time may be a factor in the etiology. Alcohol, which has been accused of being a cause of arteriosclerosis, is not now considered as such. Ruffer, in 1921, published a report of autopsies performed on 800 Mohammedans (who drink no alcohol) in which he found that arteriosclerosis was as common as in any other group.

Infections of all types, toxins, and poisons have been advanced as causes of arteriosclerosis, but very little evidence exists to support these contentions.

No discussion of the pathogenesis of arteriosclerosis would be complete without mention of the interesting studies of Wells on the colloidal constituents of the blood vessels. He feels that the occurrence of arteriosclerosis is bound up with the presence of a large proportion of elastin, which is a typical homogeneous colloidal gel. As the elastin ages, the dispersion of the colloidal particles becomes progressively less, with a reduced capacity to hold water. This leads to a decrease in elasticity and flexibility, reduced rate of diffusion and metabolism, and results eventually in a granular state of the protoplasm with a markedly reduced functional capacity. Loss of degree of tissue hydration is accompanied by changes in the colloids of the vessel wall, so that they less successfully hold in solution substances infiltrating the plasma, and calcium salts and cholesterol are 2 substances with which the plasma is most nearly saturated. The gradual change observed in the elastic fibers of arteries is only that always produced sooner or later as the natural fate of all elastic colloidal gels, and if not brought about prematurely by overstretching or local injury, it will come eventually as a manifestation of age.

TREATMENT

So far as actual treatment of the arteriosclerotic process is concerned, it can be dismissed in a few words. Some investigators have reported beneficial effects from the use of iodides, others find them useless. Anitschkow demonstrated that feeding of potassium iodide with cholesterol retarded the development of experimental atherosclerosis in rabbits. This effect was abolished by removal of the thyroid gland. Mercury and arsenic have been used but probably are of value only in sclerosis associated with syphilis. Drugs such as the nitrites have been employed in the hope that lowering the blood pressure would aid in preventing further arteriosclerosis. Electricity and baths have been utilized in this as in almost every other condition, but no one believes seriously that they have any effect on the arteriosclerosis.

PHLEBOSCLEROSIS

The question has often been asked why the sclerotic process almost always affects the arteries and very seldom the veins. The most important reason is that the arteries are exposed to much higher pressure and to greater fluctuations of pressure than the veins. The greater mechanical pressure in itself produces greater wear and tear. In addition, the compression of the vasa vasorum every time the artery is dilated by the blood pumped into it by the heart creates a condition of temporary anoxemia in the vessel wall and renders it more liable to degenerative changes. In the vein, on the other hand, the pressure is very low and the blood flow is comparatively smooth and placid. The correctness of this view is shown by the fact that well-marked sclerosis of the veins (phlebosclerosis) is often seen where there is heightened blood pressure in the veins, as in the portal system in cirrhosis of the liver, and in the pulmonary veins in mitral stenosis.

Another possible factor is the much smaller amount of elastic tissue to be found in the vein. Since both the histological studies of Jores and Wolkoff and the "aging colloids" theory of Wells have emphasized the importance of changes in the elastic layer in arteriosclerosis, it is reasonable to suppose that the greater amount of elastic tissue in the arterial wall may render it subject to more degenerative changes. Wells' statement in this connection is as follows: "An important fact is that repeated alteration in degrees of dispersion of colloidal gels or emulsions decreases their capacity to reversal towards the original degree of dispersion. This may be related to the eventual loss of elasticity of elastic fibers submitted to repeated changes in tension, especially when these changes are of extreme degree."

Levin and Bucy have recently reported a case of proliferative endophlebitis (phlebosclerosis) in which the lesions were associated with symptoms definitely indicative of impairment of venous return.

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Results in Treatment of Essential Hematuria with Moccasin Venom.—The results obtained in a series of 12 cases of proved essential hematuria form the basis for this report. The action of moccasin venom in correcting certain hemorrhagic conditions has never been satisfactorily explained although it has been assumed that there is some action on the small capillaries which makes them more resistant to extravasation of blood. For this reason its greatest value should be in hemorrhagic states in which there is vascular damage. Since injury to the small capillaries in the kidney is assumed in cases of essential hematuria, it was thought that this condition could be treated successfully by moccasin venom. . . .

The diagnosis of true essential hematuria was made in all of the cases in this series by the Section on Urology and all other accepted methods of treatment had been used without control of hemorrhage prior to the use of snake venom. Improvement was obtained in all cases . . . but in case 5 the venom was discontinued chiefly because the patient lived in an inaccessible place and could not carry out the injections satisfactorily. We have classified this case as unimproved although, during the 3 months in which venom was used, it was taken at very irregular intervals. Apparently the duration of hematuria has no relationship to the length of treatment necessary before cessation of hemorrhage occurs, for in the case of longest duration of hematuria, 16 years, the hematuria stopped (case 12) within 2 weeks and the patient has remained free from hemorrhage for 9 months. In case 4 the hematuria was only of 9 months' duration and 3 weeks of treatment were required before improvement was noted. The average duration of hematuria in this series was 4.6 years and the average length of time before bleeding ceased was 2 weeks. . . .

Extract from case report by C. H. Watkins, M.D., Division of Medicine, and G. J. Thompson, M.D., Section on Urology, *Proceedings of the Staff Meetings of the Mayo Clinic, March 31, 1937, p. 200.*

THE SIGNIFICANCE OF VASCULAR CHANGES IN THE RETINA*

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The clinician in his study of vascular disease has many methods at his command. He is able with great accuracy to examine the normal and abnormal function of the heart and its peripheral extensions. Chemical examination of the blood and urine will further enlighten him concerning vascular diseases of the kidneys. Blood pressure readings, pulse recordings, palpation and thermal changes in the extremities, will yield him information concerning the state of the larger peripheral vessels. However, the retina is the only place in the body where the blood vessels can actually be observed, and where changes in these vessels become visible in their early stages and cause functional disturbances which make the patients report to their physicians. Consequently it is of the utmost importance that internists be thoroughly familiar with the use of the ophthalmoscope so that this important information will be at their disposal. Since the retinal vessels are but prolongations of the cerebral vessels, inspection of the retina will give knowledge of great prognostic significance with respect to sclerotic changes in the arterioles of the brain, and the presence of hemorrhages and vascular degenerative changes in the retina indicate that similar changes are present in the brain tissue.

However, although a great mass of knowledge has accumulated concerning disease of the retinal vessels, the correlation of the clinical findings and histologic evidence is still in a state of uncertainty, as is also the relationship between retinal vascular disease and that occurring elsewhere in the body. It is this relationship which I shall attempt to define and formulate into a series of disease pictures. Before entering into this, however, I would first like to briefly recapitulate our knowledge of sclerotic changes of blood vessels in general. Three types have been separated, namely, arteriosclerosis, arteriolosclerosis, and Mönckeberg's sclerosis, but only the first two of these varieties have interest to us here. Arteriosclerosis is characterized pathologically by the formation of intimal plaques made up of connective tissue and wandering cells, both of which are loaded with fat, giving these plaques a yellowish appearance. In the smaller arteries these plaques may protrude into the channel for a considerable distance and thus obstruct the blood flow. In arteriolar sclerosis the primary lesion is a hyaline change between the endothelium and muscularis, with a later hyalinization of the entire media. This is a diffuse process, and high blood pressure is frequently associated with it. Bordley and Baker have attempted to show that sclerosis of the arterioles of the medulla oblongata has resulted in an insufficient blood supply and thus may be the cause of the hypertension. Also, because of the frequent association of high blood pressure and renal disease a circulating toxin or pressor substance has been sought in the blood, but such pressor substances are just as frequently found in the blood of normal individuals. MacCallum prefers to believe that some cause, as yet unknown, operates to produce hypertension, and that the violent contraction of the arterioles underlies the hyaline changes which render the narrowing permanent, and that this is associated with the alterations in the kidneys.

In the retina only the central artery has the histologic character of a true artery; namely, a well defined intima, media, and adventitia. The branches have the structure of arterioles, with an endothelial lining surrounded by a few muscle fibers and connective tissue cells. Nevertheless, the changes of both arteriosclerosis and arteriolosclerosis manifest themselves in the retinal vessels, and it is on the basis of these types that one must unravel the various retinal disease patterns.

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You have all seen an advanced degree of arteriosclerosis in elderly individuals who show no signs of hypertension and little evidence of either cardiac or renal damage. The retinal arteries will be found to be of normal caliber, but with some irregularity in the width of the blood column in the larger vessels, due to the proliferation of the intima. Also, since there has been a fibrosis of the walls, the light reflex will be somewhat irregular and the larger vessels quite tortuous. There may even be a few hemorrhages or exudates present in the retina.

Besides this group there are elderly individuals with arteriosclerosis in whom the blood pressure is found to be elevated. The fundus picture here is quite different. The larger arteries are found to be considerably constricted along their entire extent, but are quite straight. Friedenwald has carefully studied this group and has found that the constriction of the caliber of the vessels bears a close relationship to the elevation of the blood pressure. He feels that the narrowness of the vessels is due to the formation of intimal plaques in the central retinal artery posterior to the lamina cribosa, so that it is not visible in the retina and manifests itself by a narrowing of the vascular tree, with less blood passing by the obstruction. Due to the fibrosis of the vessel wall, compression of the veins occurs at the crossings, but there is no increase in the light reflex. Scattered hemorrhages and exudates occur.

The cases of so-called essential hypertension are of great importance, since they ordinarily occur in the comparatively young and progress to conditions of dire outlook. In the early stages the retinal vessels show practically no change. Often, however, spasms will be seen either localized at one point along a vessel, or traversing its length. These may persist for hours or even days, and then disappear, leaving the vessel quite normal in appearance. Mylius has studied these most carefully in the toxemias of pregnancy, and found that on termination of the pregnancy the vessels returned to the normal state. This indicates that in the early stages no organic changes have occurred in the vessel walls. However, with the persistence of the hypertension, permanent localized constrictions result from the hyalinization of the media. Volhard believes that the spastic state of the vessel causes a plasma skimming of the blood and the resultant anoxemia induces the organic changes in the vessel walls. When these changes develop they are visible with the ophthalmoscope. As hyalinization of the media progresses, the vessel walls become thicker and increasingly visible, with an increase in the width of the light reflex, caused by reflection of light from the thickened wall. The smaller arterioles become markedly tortuous, especially in the macular region. Due to the decrease in the size of the lumen of the vessels, there are irregularities of caliber along their course. Although this is a diffuse process, it does not develop equally along the entire extent of the vessels. There is marked arteriovenous compression, and later a wide variety of hemorrhages and exudates occur. This is the form so often found associated with chronic nephritis, and to which the name "albuminuric retinitis" has been given.

The confusion of terminology that has arisen around these vascular diseases of the retina results from attempting to label variations in the stage and degree of the same phenomena. "Copper-wire," "silver-wire," and "chalky" vessels all refer to the appearance of the blood vessels, and this is dependent upon the degree of hyalinization of the vessel wall. Hemorrhages are "flame-shaped" or "circumscribed" depending upon their position either in the nerve-fiber layer or in the deeper retinal layer. Their color is resultant upon the time of their occurrence, for the fresh ones are bright red, and upon aging the hemoglobin breaks down into hemosiderin with the color becoming first dusky red and then brownish. Another fertile source of confusion is the nomenclature of "exudates" in the retina. White patches are visible with the ophthalmoscope in all of the vascular diseases. They may represent various conditions which cause localized opacities in the retina. Thus the occlusion of an artery by the sclerotic process of its walls may result in a coagulative necrosis or infarct of the retina. Also, the localized disease of the vessel walls allows serum to pass out into the surrounding retina, thus causing an exudation. Similar results are produced by the faulty resorption of hemorrhages, which later undergo hyaline changes with proliferation of glial tissue and deposition of lipoids. All of these conditions may occur in any position in the fundus, although there are two sites of predilection; the macular region and the zone around the disc. Names have been assigned according to this topographic distribution, such as "circinate retinitis," "retinitis juxtapapillaris," etc. They have also been labelled according to the disease with which they are associated, as "diabetic retinitis" and "albuminuric retinitis." In the so-called typical diabetic retinitis the exudates are of a solid and clear-cut appearance, although in long standing cases this is rare. That these exudates depend on the vascular disease rather than the presence of acetone bodies or increased sugar in the blood, is made evident by the fact that they are absent in youthful severely diabetic patients, while they are common in elderly individuals who have only a moderate degree of diabetes. Similarly, in chronic nephritis the retinal exudation is not dependent upon the renal damage and nitrogen retention, but again upon the local vascular disease in the retina. We often see young patients in uremic coma who have no retinal lesions, while older people with moderate kidney damage may have the well-developed picture of "albuminuric retinitis." This is characterized by the star-shaped pattern of exudates in the macular region. The star shape of the exudates is the result of the stasis in the veins draining the macula, so that when fluid seeps out into the retina, it is confined along ridges by the supporting glial structures of the retina. It is thus frequently seen also in papilledema from brain tumors, where venous stasis results from the increased intracranial pressure, without vascular disease being present.

A further confusing factor is the great tendency to thrombus formation in the retinal veins during the course of arterial disease. Koyanagi has explained this on the basis of an intimate fusion of the arterial and venous walls at the points of crossing, so that atheromatous changes on the arterial side of the intima extend into the veins and thus allow the slowly moving venous blood to thrombose. If only a branch vein is thrombosed, the resultant hemorrhage will be distributed along the course of the retina drained by this branch. When the central vein, however, is occluded, the hemorrhage will be splattered over the entire retina in a most extraordinary manner. The retina will appear to be permanently damaged, but in a number of these cases the thrombus can be recanalized, and when the hemorrhage is absorbed good vision will return. A larger number of these cases develop a severe secondary glaucoma several months after the onset of the thrombosis, and this type of glaucoma yields to no medical or surgical treatment, so that enucleation must usually be performed.

The literature upon the subject of vascular diseases of the retina is enormous, and I have not attempted to cover the entire field. Much is unknown, and much is hypothesis. I have only attempted to correlate some of the patterns and make it useful for the clinician in his practice.

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Water Metabolism.—. . . to maintain the water balance of a patient who cannot use his gastro-intestinal tract, allow two liters for the loss through vaporization, one and one-half liters for the urine and add to this a quantity equal to whatever amount he is vomiting or otherwise losing. Secondly, if a patient comes to you dehydrated as from vomiting, give him fluid equal to 6 per cent of his body weight and then carry on as with a patient whose water balance you are maintaining. Loss from the gastro-intestinal tract should be replaced by a physiological saline solution and the remainder of the fluid given as 5 per cent dextrose in distilled water.

Extract from article by Frederick A. Coller, M.D., Ann Arbor, Michigan, *Journal, Indiana State Medical Association, April, 1937, p. 177.*

THE MINIMIZING OF PSYCHIC TRAUMA IN INDUCTION OF ANESTHESIA IN CHILDREN

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The effects of the emotions on the body metabolism are factors which may influence it for good or evil. It is desirable to place a patient in the optimum psychic state with other essential preparations for operation. Panic or depression before operation has been observed to create a poorer risk. Failure to adjust psychically following an operation has occurred. This may take the form of a psychosis or neurosis. Mild sedation is not enough since conscious control over fears is often lost and the patient is more unmanageable than ever. Psychic trauma caused by the unguarded remarks of the hospital personnel on imaginative patients should be guarded against. Consider also on such a person what a mechanical, chilly, anxious or hurried attitude may mean.

Properly administered, induction of anesthesia in children should be without the child knowing that anything unusual or untoward is occurring. It should avoid instilling in the child a terrorizing memory to frighten it throughout the rest of its life or when subsequent anesthetic experiences may be necessary.

It is the contention of some anesthetists that the anesthetic process should be explained to children before operation. To my mind it is doubtful if this is wise in the great majority of instances. However, children old enough to understand what is meant by anesthetic, even in its simpliest meaning, may be instructed, but not by the parents. If the induction is carried out as outlined there is nothing unpleasant to experience and hence any warning or hint of unpleasantness only adds to the natural apprehension at the sight of the anesthetist, hospital personnel and apparatus.

The general conduct should be cheerful without too much talk. Attention by the anesthetist to the smallest detail is obviously most highly essential in effecting successful induction. Habit in proper procedure, all cases being given the same attention, should give the experienced an appreciation and understanding of what causes child fright in the ordinary nitrous-oxide induction procedure.

Three troublesome features common in the induction of children, any one of them capable of preventing smooth induction, are darkness, the smell of ether, and restraint.

In the first instance, the eye shield should never be placed until after induction. This is a common mistake and tends to frighten the child at the onset.

In the second, namely, the smell of ether, this should be immediately combated by freeing the machine of all ether odor. When the gases are started flowing it is sometimes possible that the child's attention may be distracted to this procedure by the anesthetist. He may thus be made interested in something new and strange, and while he is forgetting his fears, the anesthetist is freer to ascertain by his olfactory sense that the machine is free from ether and other odors. Nitrous oxide is of course almost odorless even if with a faint sweet smell, and should be allowed to flow until all other odors have been supplanted.

The face piece may now be held in plain view so that the patient can see that it is nothing to be feared. Then it should be lowered until the gases are passing over his face to the partial exclusion of air. Anesthetization of the child can often be accomplished without the mask being held close to his face.

Minnitt of Liverpool, England, describes an interesting method of inducing anesthesia with nitrous oxide with the aid of "traffic lights" or colored discs attached to the mask, by gradually lowering the mask while the child's attention is attracted to the "traffic lights."

As nitrous oxide is heavier than air, it passes over the face, while displacing the air to a large extent. Ether may be added to the gases after signs of a light anesthetic are present and the child has been successfully induced without restraint.

Restraint is sometimes necessary if the child has already been frightened from a previous experience, or if there is present an unsympathetic understanding of the child's mentality. Sometimes a child is so spoiled that it objects to every effort in its interest on the part of the anesthetist, especially if the parents are present. The attitude of the child is more often than not a reflection of its training.

Avertin and certain of the barbiturates have come as a blessing to these spoiled and otherwise excitable children and should be used in these cases when possible. The point is made, however, that premedication is not always necessary if more attention is given to the small details of induction.

As examples of what may be accomplished by using these simple methods, one mother stated that her 6-year old child did not remember having been anesthetized; a 7-year old boy did not know he went to sleep; and a 9-year old girl greeted the anesthetist with a smile and said that she would not mind another anesthetic. A 13-year old boy who had been anesthetized 5 years before and had been very much frightened especially of "having my eyes covered," when reassured on this point and also that nothing would be placed over his face became calmer and was anesthetized without his moving and without restraint. The next day he said that he did not mind that anesthetic since he only received gas, whereas after induction he had been carried along on drop ether.

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LEGAL RESPONSIBILITY INCIDENT TO DIAGNOSIS AND TREATMENT*

Frederick A. Fenning

General Counsel for the Society

I speak with particular reference to the legal responsibility incident to diagnosis and treatment, and shall not dwell upon malpractice suits. I want to emphasize the relationship existing between physicians and their patients and the public at large.

The people are entitled to assume that every licentiate possesses certain fundamental knowledge of his profession. A licentiate may disclaim his ability to diagnose or treat any particular disorder and by so doing and refusal to act he protects himself against "backfire," but if he makes a diagnosis he has assumed a definite responsibility, since as just pointed out the patient is justified in placing reliance upon a diagnosis made by a licentiate. Diagnosis is a scientific determination, and in one jurisdiction, at least, it has been held that diagnosis may be established solely by acts and conduct; also, it has been held that a physician is liable for a negligent diagnosis although no treatment is rendered.

What then is the proper rule of conduct for the doctor who suddenly is confronted with a condition as to which he is uncertain in his own mind? If it is a condition falling in a branch of medicine or surgery which he believes himself to possess the ability of the average practitioner in that branch to handle, then he determines his course by the exercise of his best judgment. The medical profession will approve, and the law will save him harmless, for judgment is not infallible, and errors of judgment made by competent men have occurred from the beginning of time. On the other hand, if, cognizant of his lack of knowledge or experience along the particular line, he nevertheless undertakes diagnosis or treatment, he has assumed what may turn out to be a heavy burden, since in the final analysis he simply has made a guess, and diagnosis as a scientific determination must be based on judgment, which never is formed by guess.

If the doctor is confronted by an emergency presenting conditions or complications outside his line of professional activity, he will render first aid in accordance with his best professional judgment. Further than that, if he is thoughtful of the welfare of the patient and of his own personal interest, he will refrain from expressing any opinion. In such circumstances, again in the interest of both patient and physician, the latter should advise that the former go to a hospital or to a medical man qualified to give proper attention.

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* Read before the Society, January 27, 1937.

It is relatively easy for a physician or a surgeon to protect himself by advance precautionary measures. It is infinitely more difficult for him to undertake to defend or justify professional advice or opinion that has been called into question.

May I illustrate by referring to a case which came under my personal observation and which I have remembered both because of the manner in which the physician protected himself and the fact that the patient not only was not harmed but was properly directed.

A young man broke a bone in his forearm while cranking a motor boat off the coast of Maine. He was taken to shore and to the only doctor in a town of 700 people. The country doctor at once said that with his facilities he could not determine the kind of fracture that had been sustained nor would he undertake to set the bone. He said that he would make the patient more comfortable by applying a splint and bandage (which he did) and then advised that the patient go to a general hospital at Bangor some 55 miles distant. The next day at Bangor it was found by X-ray examination that the broken ends of the bone were not in juxtaposition, and with fluoroscopic aid the bone was properly set. Had the country doctor proceeded to set the bone and given any assurance that he had so set it the resulting condition undoubtedly would have properly subjected the doctor to a suit for damages. Moreover, far greater detriment would have come to the young patient in the improper setting of the broken bone.

Coming now to the responsibility incident to treatment, there is a general rule that a physician's error in judgment in treating a patient does not amount to malpractice. This rule, however, has no application in a case in which the error of judgment is so gross as to be inconsistent with the degree of care and skill that the operator should possess. Here, again, we find adherence to the principle that the public is warranted in placing reliance on licentiates, and if the licensed physician or surgeon actually undertakes to treat a patient the latter will be protected against improper treatment and lack of skill. By this is meant, of course, that the patient can bring an action against the physician. As was pointed out with respect to diagnosis, so also is it the fact as to treatment that a physician can disclaim familiarity with the subject and therefore decline to give treatment; but if he does give treatment he must be prepared to defend and justify the same.

To sum up this brief discussion: When a licensed practitioner undertakes diagnosis or treatment he assumes a definite legal responsibility. This is because of the duty he owes the public in return for the license which public authorities have issued and under which he practices. If he possesses a reasonable degree of knowledge and skill and exercises reasonable judgment he may expect the protection of the law. A man who lacks sufficient knowledge of a particular disorder cannot form a proper degree of judgment and hence should refrain from making a diagnosis or prescribing treatment.

The Treatment of Erysipelas by Ultraviolet Ray.—. . . It may be noted . . . that the superficial bactericidal action is sufficiently pronounced to render it safe to allow cases of erysipelas to remain in wards with other patients. Devine reports that in 10 years' experience with ultraviolet therapy in erysipelas in the Veterans' Facility in Whipple, Arizona, there has been no spread from any case, and in the Presbyterian Hospital in New York cases are allowed to remain in the wards, and are taken off infectious precautions in 48 hours.

The effect of ultraviolet light on the patient with erysipelas is sufficiently marked as to be somewhat spectacular. The beginning of improvement in the patient coincides with the development of the erythema, which occurs in from 2 to 8 hours following treatment. Relief from discomfort, drop in temperature, and limitation of spread of the lesion may be expected from the first exposure, provided the dosage is sufficient. . . .

Conclusions.—The ultraviolet ray seems to be the treatment of choice for erysipelas, from the standpoint of rapid control, safety, and economy to the patient. It shortens the period of hospitalization, eliminates the necessity for isolation, and has considerably lowered the mortality rate. The optimum dosage is just short of vesiculation.

Extract from article by ANNETTE M. BIEKER, M.D., St. Petersburg, *Journal, Florida Medical Association, March, 1937, p. 427.*

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SURGICAL VERSUS NON-SURGICAL TREATMENT OF RENAL TUBERCULOSIS

The invention of the cystoscope[1] and its development into a means for practical catheterization of the ureters[2,3] together with the discovery of the tubercle bacillus[4] placed the diagnosis of renal tuberculosis on a firm footing for practical clinical purposes. Postmortem and clinical findings[5,6,7,8] demonstrated that the caseo-cavernous form was generally unilateral, in the early stages at least, and that it was susceptible of cure in a majority of instances by nephrectomy. Even in instances in which both kidneys were involved certain authors[9] did not hesitate to recommend removal of the more diseased one, justifying the operation on the basis of the definite although often temporary improvement that occurred in the painful bladder symptoms.

The increased general efforts against tuberculosis that were current in the first decade of this century undoubtedly did much to lower the incidence of renal involvement and brought cases to a definite diagnosis earlier.

The invention of pyelography by Voelckler and von Lichtenberg in 1906[10] put another diagnostic means at the command of the urologic surgeon.

Since 1924 the experimental and postmortem studies of Medlar[11,12] and the clinical investigations of sanatorium patients by Thomas and Kinsella[13,14] and intervening papers have indicated that renal tuberculosis exists in forms that tend to heal, that may exist for a long time without evoking the clinical symptoms or the signs ordinarily considered essential to diagnosis (cystitis, albumin and pus in the urine) and that are commonly bilateral. Although it has not been shown that a healing process can go on to complete cure in the caseo-cavernous form of the disease in the human kidney, a balanced immunity may be struck and held, in some instances for long periods, during which the patient may suffer little or no local discomfort and apparently be in a very good state of general health. The reverse of this, that the disease, once established, is ordinarily steadily progressive and tends to involve the other kidney or to become disseminated in the majority of instances, is also true.

That the kidney lesions of tuberculosis might exist without giving diagnostic symptoms or signs was to have been expected had thought been given to the matter; such a stage would correspond to the incubation period of a more acute infection with a better understood, more rapid and definite evolution. It required a painstaking, laborious piece of clinical and pathologic work in a sanatorium, where the incidence of such a preclinical stage would be expected to be high, to demonstrate its existence. Considering the preponderance of evidence that renal tuberculosis is always secondary and generally hematogenous, the wonder is that it is

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so often unilateral and so seldom bilateral. No theoretical explanation or experimental work has been adduced to explain this satisfactorily, so that, until more is known, one must be content with noting the observed fact and acting upon it. However, much is known of tuberculosis, only enough is understood to obscure our ignorance of the parts not yet revealed and demonstrated.

From a practical viewpoint the method of handling a patient with caseo-cavernous renal tuberculosis at present remains about where it was 15 years ago—nephrectomy, if the disease is unilateral, followed by rational care in a sanatorium or at home, under the care of a competent phthisiologist afterwards. The circumstances under which latency of symptoms or regression of the lesions may be brought about are too uncertain to chance the risk that it entails. Under non-surgical treatment alone the best that may be hoped for is an asymptomatic, latent but not innocent, closed lesion which may break down at any time, the patient being kept as a semi-invalid for an indefinite period in order to attain or maintain this uncertain status. When this is contrasted with the results of prompt nephrectomy in unilateral instances of the caseo-cavernous form (*Operative Mortality* 5.6 per cent of 2,752 assembled cases—*Ten-year Cures* 53.9 per cent of 330 assembled cases[15] after which the patient is usually entirely well and ready to assume his customary occupation within a month or two after operation, the choice between the two methods of treatment should not be difficult. Even if a deliberate or accidental mistake is made and a tuberculous kidney is removed in the presence of a minor infection on the opposite side, the patient may gain relief from his disturbing bladder symptoms and be in a better position to profit from the regimen of rest, hygiene and hyperalimentation customarily prescribed for forms of tuberculosis other than renal.

The moot question of whether a tuberculous lesion is ever cured in the sense that other infectious diseases are, with complete destruction of the infecting bacteria and return of the tissues to an approximate normal[16, 17] would make it seem desirable to completely remove an infected organ whenever possible, rather than to let it remain as a possible source of dissemination for an indefinite time.

R. M. LeC.

REPORT ON AMERICAN MEDICINE BY THE AMERICAN FOUNDATION FOR STUDIES IN GOVERNMENT

There has just been published by The American Foundation for Studies in Government a voluminous report entitled "American Medicine. Expert Testimony Out of Court." The report is in reality a massive collection of quotations from 5,000 letters from 2,100 physicians. The physicians whose letters are quoted represent general practitioners, all types of specialists, public health officers, deans of medical schools and hospital administrators in both governmental and private institutions, and they are scattered through every state of the Union in both urban and rural localities. The letters were sent to the American Foundation in reply to the following question:

"Has your experience led you to believe that a radical reorganization of medical care in this country is indicated? If so, in what direction? If you do not believe that radical reorganization is indicated, what, if any, changes or revisions in the present system would you like to see made? What evolutionary possibilities would you stress?"

The report consists, as stated above, very largely of quotations from the 5,000 letters received in reply to the above questions, but with connecting explanatory remarks by the editors. The editing has been done with great skill and discrimination and with no attempt to draw conclusions or to formulate recommendations.

The nature and purpose of the report is explained in the following quotation from the "Foreword" written by Truman G. Schnabel, M.D., Chairman of the Medical Advisory Committee: "It will be impossible to read this report profitably unless it is borne constantly in mind that the purpose of our inquiry was not to poll the medical profession upon anything whatever, but rather to assemble ideas, to etch in the whole picture. It is true that the results of the inquiry do indicate roughly certain 'trends,' but it is questionable whether anyone could with integrity state these in the form of conclusions. Many of the most profound and careful thinkers among our correspondents are explicit in stressing the very tentative nature of their views. They are weighing and considering and often changing. If our inquiry had asked for 'votes' for this or against that, I am confident it would have been relegated to the waste basket. Our correspondents wrote frankly because they were not asked for conclusions, and because they were invited to think out loud. They knew we should not list them as advocates or proponents of an idea. They contributed their experience, their impressions, and their observations richly—without positivism. We are endeavoring to present them with a reciprocal lack of positivism, and with no attempt to attach rigid conclusions to fluid thinking.

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"The intent and purpose of this report is to illuminate and not to prove. Those who hoped for a numerical report that so many are for 'state medicine' and so many against it will be disappointed. The material that has come through to us is adapted to no such superficial handling. The letters are, in the main, the mature and profound and poignantly sincere thought of men in the field who recognize that there is a problem of subtle composition and who would like to see it solved not by facile experimentation on a broad and untried scale but by experiment guided by all the resources both of science and of statesmanship."

The subjects treated in the letters which are the basis of the report cover nearly all of the socio-economic aspects of medical care and public health which have been under general discussion for the past few years. The editors have arranged them under the following chapter headings:

I. Is adequate medical care now generally available?
II. Views on general principles and considerations that should underlie the organization of medical care.
III. Medical education.
IV. Specialization.
V. Group practice.
VI. The place of the hospital.
VII. Public health organization.
VIII. Experimentation—state, county and community plans.
IX. State medicine.
X. Health insurance, compulsory, voluntary, hospital, industrial.
XI. Limited state medicine and private practice.

Although the report is composed of innumerable quotations expressing every conceivable point of view, the material is so well arranged as to make it very readable and interesting.

It will be obvious to anyone who reads the report that there is no definite, clear-cut consensus of opinion on most of the subjects discussed. One may find quoted statements there to bolster almost any shade or variety of opinion which one happens to favor. The reader is left, however, with a feeling that although there is no unanimity of opinion on a single one of the subjects there are still strong indications of the general trend of thought among those whose letters make up the report.

Without any attempt to be exhaustive the following impressions (I should not say conclusions) are strong in the mind of the present writer after a fairly careful reading of the entire report:

1. There is recognition of the fact that problems of health and medical care are bound up with many other social and economic problems. The influence of poor housing and inadequate food and shelter upon health is emphasized. It is useless to talk of "adequate" medical care when great masses of the people are "inadequately" fed, clothed and sheltered.

2. There is a very general opinion among the physicians replying to this questionnaire that there are large numbers of our population to whom modern scientific medical care is not available. This seems to be particularly true of thinly settled or isolated rural districts. There is considerable emphasis upon the opinion that

poor medical care is not always an economic question but is due to the people's predilection for quacks, cultists and patent medicines, and sometimes to inadequate training or ignorance on the part of the doctors themselves.

3. There is strong testimony to the necessity for continued change and improvement in medical education, especially for the general practitioner, and of increasing control of specialism. There is quite general approval of the newly formed national boards for certifying specialists. There are some who would like to have the examination of specialists legalized and made a state matter but the majority see great dangers in this and prefer to rely upon control within the profession through the boards.

4. Health insurance of all types receives much attention. There are those who recommend various types of voluntary or compulsory health insurance but the general trend of the recommendations is rather strongly against any type of health insurance. The opinion is very general that insurance medicine will result in lowering the quality of medical care and that so far as costs is concerned it will merely "substitute hidden taxes for direct taxes."

5. Insurance for hospitalization, in contrast to health insurance, receives quite general approval. It is strongly emphasized, however, that it is very limited in its application and that it may give rise to evils by fostering health insurance plans.

6. There are repeated proposals in the report for the tax support of hospitals and for the payment of doctors for the care of the indigent and the near indigent. This would be an important and probably highly desirable change from the present methods of haphazard philanthropic support of hospitals and no payment whatever to physicians for care of indigent or near indigent.

7. The last chapter of the report is probably the most important. It is entitled "Limited State Medicine and Private Practice." In it there is much discussion of the extent to which the state already concerns itself with matters of health and the control and treatment of disease. In the control of communicable disease, and the care of the tuberculous and mentally ill, state medicine is already a fact. Other diseases, notably syphilis and cancer, are strongly recommended for complete state care, while there are a considerable number who think that chronic diseases that require long hospitalization, such as arthritis, should be cared for by the state.

It is repeatedly emphasized in this chapter that it is practically impossible to keep curative and preventive medicine separate. The state is becoming increasingly concerned in the treatment of disease, while the private practitioner must become increasingly concerned with the prevention of disease. It is the quite general opinion that efforts in the immediate future should be toward better coördination of the work of public health departments with that of the private practitioner, with a realization that their work must overlap in many fields of medicine, both preventive and curative.

Altogether the report is an excellent cross-section of the medical viewpoint on many important problems of health and medical care. There is no assumption that the doctor alone can solve all of these problems but it seemed to the American Foundation "that the group best qualified to define the problem in the first instance is the qualified medical men of the country."

It seems fair to say that in answer to the original question propounded to the doctors "Has your experience led you to believe that a radical reorganization of medical care in this country is indicated?" the answer is preponderantly "No, but evolutionary changes are necessary which will strike the proper balance between state control and private practice."

A. C. C.

MEASLES IN WASHINGTON
1937–1938

Probability of Increased Incidence

The periodicity of measles in this community has been well known to those interested in child health. Dr. James G. Cumming, Epidemiologist in the Department of Health, has called attention to the fact that we may look for high points in a recurrent measles frequency every third year. The last high point having occurred in 1934, would place the recurrence in the present year. While the summer months of the year will show the usual drop in the frequency of cases, we may expect an increase during the fall months, carrying us possibly over into the year 1938. Inasmuch as it is possible to forecast the recurrence of epidemics of certain diseases, it is proper that this should be brought to the attention, not only of the profession but also of the public. Measles unfortunately is not quite the harmless childhood disease which it is commonly believed to be, but by reason of complications measles is a disease that, particularly in the early-age group, should have medical supervision. Human immune blood serum, or whole blood, and lately placental extract have proved quite effective as preventive agents. It seems that we are facing an opportunity to establish the worthwhileness of these biologicals offered for immunization against measles, respectively, modifying the attack.

The Health Officer, Dr. George C. Ruhland, suggests that where immunizing agents are used, careful record should be kept. It would seem more advantageous for the immunizing agent to be used with view to modifying the attack rather than entirely preventing the infection.

In combating a known recurrence of measles three things seem especially important: *(1) To arouse the public, especially those families having children in the dangerous-age group; (2) to secure the coöperation of the medical profession; (3) to develop the departmental machinery, i.e., especially the nursing staff.

The Medical Society of the District of Columbia, through its Committee on Public Health, will, it is assured, participate in the organization of plans for lessening the morbidity and mortality curves of measles during the current year.

COMING MEETINGS

Annual Scientific Assembly

May 5–6

The General Chairman, Dr. Joseph Horgan, with his Subcommittee Chairmen, has prepared a program and a series of events for this year that should eclipse previous meetings both in the way of interest and attendance. Tri-state Day, Wednesday, will, it is believed, bring to Washington large numbers of our friends in the profession from neighboring communities in Maryland and Virginia. A special program has been prepared for visiting ladies; announcements will be made at registration desk. Get a program if you have not received yours; read of the many opportunities to increase your fund of knowledge meanwhile creating pleasant social contacts. Members of the Medical Society of the District of Columbia are especially urged to write to confreres in Maryland, Virginia, West Virginia and other nearby states. All are assured a hearty welcome. No registration fees. Complimentary luncheon at the Mayflower Hotel for registrants on Wednesday, A.M., May 5. Don't fail to *register*.

Subchairmen:

Daniel F. Lynch, *Associates*
Charles H. McEnerney, *Attendance*
John D. Wynkoop, *Banquet*
Stuart O. Foster, *Medical Clinics*
W. Warren Sager, *Surgical Clinics*
W. Preston Haynes, *Entertainment*
P. A. McLendon, *Finance*
B. F. Dean, Jr., *Halls and Exhibits*
P. S. Constantinople, *Luncheon*
Raymond W. Murray, *Printing*
B. W. Leonard, *Program*
George K. Nutting, *Public Meeting*
W. W. Chase, *Publicity*
Coursen B. Conklin, *Registration, Advertising and Technical Exhibits*
Alec A. Preece, *Woman's Auxiliary Liaison*
Ella M. A. Enlows, *Women Physicians*

Program Synopsis

Wednesday, May 5, 9 A.M.

Registration.

Scientific Session.

"Paraldehyde-benzyl Alcohol Obstetrical Analgesia by the Kane-Roth Method." Howard P. Parker, M.D.

"Learning Disability in Intelligent Children—A Symptom of Emotional Disturbance." Agnes B. Greig, M.D.

"Neurodermatoses." F. J. Eichenlaub, M.D.

"What the Health Department is Doing in the Prevention and Treatment of the Venereal Diseases." T. C. Thompson, M.D.

"The Early Diagnosis and Significance of Retinal Vascular Disease." Benjamin Rones, M.D.

"The Socialization of Medicine: To What Extent is it Desirable?" Arthur C. Christie, M.D.

Wednesday, May 5, 12:30 P.M.

Complimentary Luncheon for *all* who *register* Wednesday, A.M.

Guest Speaker: Arthur Deering Call, Ph.D.

Subject: "As to the Prospects for War."

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* Ruhland, G. C., and Silverman, A. C.: What Can We Do About Measles? Am. J. Pub. Health, 1928, **18**, 131.

Wednesday, May 5, 2 P.M.

Scientific Session—Tri-state Afternoon.

"The Operation of a Small Community Hospital." J. W. Bird, M.D.

"The Sympathetic Nervous System in Relation to Cardiovascular Disease." James C. White, M.D., Boston, Mass. (guest speaker). Dr. White is a graduate of Harvard School of Medicine, 1923; Moseley Traveling Fellow, and Assistant Professor and Tutor in Surgery, in his alma mater; Ex-resident in Surgery, and Assistant Visiting Surgeon in the Neurological Service, Massachusetts General Hospital.

"The Problem of Appendicitis." Harry H. Kerr, M.D.

"Artificial Fever Therapy of Gonorrheal Arthritis." Henry B. Gwynn, M.D.

"The Value of Chest Leads of the Electrocardiogram in Cardiac Diagnosis." Thomas S. Lee, M.D.

"Decompression and Autoplastic Graft in Facial Nerve Injury." William H. Jenkins, M.D.

Wednesday, May 5, 8:15 P.M.

Public Meeting.

"Medicine and the Public." Howard Wilcox Haggard, M.D., of Yale University.

Thursday, May 6, 9 A.M.

Scientific Session.

Medical Dry Clinics

"The Treatment of Bright's Disease." Paul F. Dickens, M.D.

"Clinical Observations with Protamine Insulin." Maurice Protas, M.D.

"The Value of Skin Reactions in Prognosis and Serum Treatment of Type I Pneumococcus Pneumonia." Theodore J. Abernethy, M.D.

"Chemical-biological and Clinical Behavior of Arsenoxide (Mapharsen)." George B. Roth, M.D., and George W. Creswell, M.D.

Surgical Dry Clinics

"The New Operation for Webbed Fingers." Robert E. Moran, M.D.

"Complete Avulsion of the Scalp and Loss of the Right Ear with Reconstruction by the Tube Graft Method." James A. Cahill, Jr., M.D.

"Prefrontal Lobotomy in Case of Chronic Surgical Polyaddiction." James W. Watts, M.D.

"Scrotal Hernia." F. X. McGovern, M.D.

Thursday, May 6, 2 P.M.

Scientific Session.

"Serum Therapy in Pneumonia." Francis G. Blake, M.D., New Haven, Conn. Graduate of Harvard School of Medicine, 1913, Moseley Traveling Fellow in his alma mater; Assistant Professor of Medicine, University of Minnesota School of Medicine; Associate Member, Rockefeller Institute; Sterling Professor of Medicine, Yale University School of Medicine; Physician-in-Chief, New Haven Hospital and New Haven Dispensary.

"The Surgical Treatment of Mental Disorders." Walter Freeman, M.D., and James W. Watts, M.D

"Chemotherapy of Bacterial Infections with Sulfonamide Compounds." Sanford M. Rosenthal, M.D.

"Mandelic Acid: The New Urinary Antiseptic." H. A. Fowler, M.D.

"Physiological Response to Massive Infusions of Physiological Salt Solution." R. A. Cútting, M.D., Ph.D.; A. M. Lands, Ph.D.; and P. S. Larson, Ph.D.

"The Use of Acacia in the Relief of Edema in Lipoid Nephrosis." John H. McLeod, M.D.

"Present Day Treatment of Tuberculosis in the Sanatoria of the District of Columbia." J. Winthrop Peabody, M.D., and Daniel L. Finucane, M.D.

Thursday, May 6, 7 P.M.

Banquet, Mayflower Hotel.

In addition to papers there will be a comprehensive scientific exhibit and a technical exhibit in the Library. Numerous cinemas depicting various phases of medicine and surgery will be exhibited.

American Medical Association meets in Atlantic City, June 7–11. Prepare now to go. If you are not a Fellow, apply to the American Medical Association headquarters. Qualify now. The Medical Society of the District of Columbia wants the registration of the highest percentage of Fellows of any constituent state society. If you are an Active Member of the Medical Society of the District of Columbia and not a Fellow of the A. M. A., immediately get in touch with your Society's office and learn how fellowship may be accomplished. The scientific papers, the exhibits, and above all the opportunities for friendly contacts in the delightful surroundings of a seashore resort city will attract in all probability the largest attendance noted at these meetings. Make your hotel reservation now.

American Medical Golfing Association announces the twenty-third annual tournament at beautiful Seaview Country Club, Atlantic City, N. J., on Monday, June 7. There will be 70 trophies and prizes; 36 holes of golf to be played in competition. All male Fellows of the American Medical Association are eligible and cordially invited to become members of the American Medical Golfing Association, 2020 Olds Tower, Lansing, Mich.

Fifth International Congress of Radiology convenes in the Palmer House, Chicago, September 13–17, 1937. Dr. Arthur C. Christie, President of the Congress which is expecting 500 or more distinguished guests from a score of European countries as well as from the continental Americas, states that conjointly the America Roentgen Society, the American College of Radiology, the Radiological Society of North America, and the American Radium Society will meet. The First International Congress was convened in London in

1925 and triennially since. Dr. Benjamin H. Orndoff, General Secretary of the Congress, has headquarters at 2561 North Clark Street, Chicago, Illinois. Other officers: Honorary Vice Presidents, Drs. George E. Pfahler of Philadelphia, James Ewing of New York City, and William D. Coolidge of Schenectady; International Executive Committee, Drs. Arthur C. Christie of Washington, D. C., Chairman, C. Thurstan Holland of Liverpool, Gosta Forssell of Stockholm, Antoine Beclere of Paris, Hans R. Schinz of Zurich, Karl Frik of Berlin, Mario Ponzio of Turin, Italy, Tamotsu Watanabe of Osaka, Japan, Heliodoro Tellez-Plasencia of Santander, Spain, and Gottwald Schwarz of Vienna.

American Association on Mental Deficiency meets in Atlantic City, May 5–8, 1937; Headquarters, Haddon Hall. Many papers and scientific discussions will be given on the cause, care and prevention of mental deficiency. All interested should note these dates.

The American Board of Ophthalmology will conduct an examination in PHILADELPHIA, June 7, and CHICAGO, October 9, 1937. All applications and case reports, in duplicate, must be filed at least 60 days before the date of examination with Dr. John Green, Secretary, 3720 Washington Boulevard, St. Louis, Mo.

NEWS AND PERSONALS

May Day is Child Health Day. Dr. Ella Oppenheimer, Chief of the Bureau of Maternal and Child Welfare, Health Department of the District of Columbia, is the chairman of a committee for local observance of this national event, which is held in accordance with a Congressional resolution of May 18, 1928, and sponsored by the United States Children's Bureau. On this committee numerous members of the Medical Society of the District of Columbia serve; inclusive are: Drs. George C. Ruhland, Health Officer; Hugh J. Davis, Clinical Director of Child Welfare, Health Department; J. Bay Jacobs, Clinical Director of Maternal Welfare, Health Department; William Mercer Sprigg, President, Medical Society of the District of Columbia; P. Herbst, Jr., Herbert P. Ramsey, Joseph A. Murphy, etc. Each year an appropriate slogan is brought forth with an implied objective. The 1937 suggestion is "*Health Protection for Every Child;*" the objective "*to promote the extension of year-around child health service, including services for physically handicapped children in every community.*" The District of Columbia Congress of Parent-Teacher Associations has yearly featured and stressed the examination of the pre-school child. The local profession has generously participated, rendering service without thought of monetary reward. It stands ready to further the movement and coöperate fully to the end that much will be accomplished for our future citizenry.

The American College of Physicians convened in St. Louis, Mo., April 19–23, 1937. Results of election: Drs. William J. Kerr, San Francisco, President-elect; David P. Barr, St. Louis, First Vice President; G. Gill Richards, Salt Lake City, Second Vice President; William Gerry Morgan, Washington, D. C., retiring Secretary-General, Third Vice President; George Morris Piersol, Philadelphia, Secretary-General; William Stroud, Philadelphia, Treasurer. Dr. James H. Means of Boston was installed as President. The Executive Secretary is Mr. E. R. Loveland, Philadelphia. Members of the Medical Society of the District of Columbia who participated in the scientific program of the College:

DR. WALTER FREEMAN gave a clinic on "The Application to Clinical Neurology and Psychiatry of More Recent Anatomical and Physiological Studies of the Nervous System," at the Barnes Hospital.

DR. WALLACE M. YATER, jointly with Dr. M. J. Schapiro, gave a paper entitled, "Ebstein's Disease of the Heart or Congenital Dislocation of the Tricuspid Valve."

Dr. Vincent du Vigneaud, Professor of Biochemistry, George Washington University School of Medicine, has been awarded the Hillebrand Prize for 1936 by the Chemical Society of Washington. The award, which was formally presented on March 11, was made in recognition of Dr. du Vigneaud's contributions to the chemistry of biologically significant sulphur compounds.

Dr. Wallace M. Yater will read a paper, entitled "Maintenance of the Functional Integrity of Occluded Large Arteries as Demonstrated by Thorotrast Arteriography," before the American Society for Clinical Investigation in Atlantic City, N. J., May 3, 1937.

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THE USE OF SULFANILAMIDE IN THE TREATMENT OF GONORRHEA

REPORT OF RESULTS IN ONE HUNDRED CASES

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The substance Sulfanilamide, which is the name adopted by the Council on Pharmacy and Chemistry of the American Medical Association for para-aminobenzene-sulfonamide, was first brought to my attention about the middle of December, 1936, through a thrilling report before this Society of its use by Dr. Prentiss Willson in a case of pelvic infection and septicemia with Streptococcus hemolyticus. The following day I observed the effect in a case of meningitis following mastoiditis, in which the same organism was the offender. Since chemotherapy has long been a strong arm in the treatment of infections of the genito-urinary tract, Dr. J. M. Fadeley and I investigated the substance with the idea of using it in the treatment of gonorrhea.

It was decided that a group of 100 cases of all degrees and stages of infection with the gonococcus were to be accumulated and at the end of that series an evaluation made of the results and effects obtained. This series began on December 21, 1936, when the first case was treated, and ended May 1, 1937. The following report is a preliminary one, setting forth only the gross observations, the more technical ones to be reported later.

In all cases smears of the urethral discharge were made by two or more examiners in order to verify the diagnosis. The urine examinations were made in the 2-glass test, supported by the microscope. The cases were divided for purposes of convenience into new and old infections instead of acute and chronic.

New cases are those which were seen within 2 weeks of the onset of urethral discharge, and consisted of both previously treated and untreated cases. Old cases are those which have had their infection for 2 weeks or more, and all of these previously had the conventional varied treatment for gonorrhea. Of the new cases 75 per cent showed pus in both glasses and varying degrees of mild prostatitis. Nearly all of them had burning and discomfort on urination.

All of the old cases had pus in both glasses and a varying degree of prostatic infection, from moderate to severe, besides the urgency, frequency and burning on voiding which is associated with inflammatory processes of that part. No case developed epididymitis. Two cases arriving with epididymitis promptly subsided in less than 48 hours, beginning to do so in 24 hours with disappearance of pain and swelling.

It was interesting to note that although several cases showed no response to treatment with Sulfanilamide so far as the clinical evidence was concerned, they did not show, on the other hand, any tendency to get worse and remained stationary. It was felt that perhaps these cases were destined to be of that fulminating severe type in which, regardless of the physician's best efforts, all of the complications would perhaps follow, but that some protection was offered by the chemical agent. Associated with the administration of Sulfanilamide were observed a long list of by-effects, chiefly a profound weakness and fatigue, indescribable epigastric sensations called "indigestion," not associated with nausea or vomiting. Several persons described a sensitiveness of the skin of the lower extremities, and one of these very definitely insisted that there was a marked slowing of and loss of force to the urinary stream. In this patient the skin sensation of the lower extremities was very marked, associated with a "tingling" of the toes. All of these and other minor side-effects disappeared in from 24 to 48 hours after discontinuance of the agent. We were unable to recognize any external or gross evidence of methemoglobinemia or sulphemoglobinemia. The time of onset of these symptoms varied, but most cases began to complain when they had taken between 60 and 80 grains. In no case was the patient prepared for these symptoms by suggestion, the report being purely spontaneous in each case.

An observation of great interest was that it became possible to predict the cases in which the result would be successful. Those who complained early and bitterly of the side-effects gave the best response to the treatment, while the cases which are counted as failures apparently had a great tolerance for the drug or did not react to it in that yet unknown manner by which it produces its best effect.

Many detailed observations remain to be interpreted. The time of recovery might in many cases be even more rapid than we know, since it has not yet been accurately determined when treatment should be safely discontinued. One case cleared in 24 hours and medication was discontinued. The gonococcus-laden urethral discharge recurred within the next 12 hours. Treatment was resumed for a second 24 hours and the patient has remained 'cured' for 3 months. The patients were not seen every day, there being an intervening day between visits. Symptoms of dysuria and other urethral and bladder distress ceased in 12 to 24 hours.

Of the new cases having a clear second glass of urine and no prostatic infection all were free of urethral discharge with a pus-free urine in the first specimen microscopically in 24 hours except 1 case. This case became one of the most intractable cases I have seen for a long while, although there have been no complications. All of these cases have remained pus-free from $4\frac{1}{2}$ months to 2 weeks. Many of them complained of severe urethral itching for several days after treatment had ceased, but this was promptly relieved by the methods employed to determine the cure. In 1 case in this group recurrence followed discontinuance of treatment, but response was prompt in another 24 hours and recovery ensued.

The new cases in which there was pus in the second specimen and mild prostatitis showed the usual prompt relief of symptoms and simultaneous clearing of the second specimen within 48 hours. The first specimen cleared gradually over the following 48 hours and in most instances was clear and remained so in 5 to 7 days. One patient in this group became progressively worse and after 6 days did not return, and a second one resisted treatment and has joined the ranks of the failures. The prostatic infection in all of these cases disappeared promptly and required no additional treatment. Although some of the cases in the group called old cases responded more slowly, most of them showed the same startling behavior as the previous group, such as subsidence of symptoms, clarification in second-glass test and cessation of urethral discharge. If the treatment was at all successful the urine became crystal clear in both glasses within 10 days in the longest case and 5 days in the shortest case, by the same criterion. There seems to be a tendency to carry a few shreds in the first specimen for several days after clarification and residual pus in the prostate from 1 plus to 2 plus. This, however, soon disappears on follow-up treatment designed to overcome it.

Seven cases of the old-case group have defied treatment and refuse to respond to any treatment.

Of the 40 cases of group 1, the new cases treated with Sulfanilamide, there were 3 cases, or 7.5 per cent, in which the treatment failed. In group 2, or the old-case group with 60 cases, 7, or 11.5 per cent, failed. The average length of time for a clinical recovery was 5 days. In other words, 92.5 per cent of the fresh cases and 88 per cent of the previously treated cases recovered.

The treatment consisted of the administration of 40 grains of Sulfanilamide daily, 10 grains after each meal and 10 grains at bedtime. Twenty-four tablets were prescribed or enough for 3 days from which no serious side-effects were expected, and the patient was seen every other day, at which time a complete check-up as to urethral discharge, urinalysis, prostate and general symptomatology was made. When indicated, at the termination of the use of Sulfanilamide, a few of the conventional genito-urinary treatments were given to clarify the residuals. The criterion for cure was the disappearance of microscopic pus from the urine, absence of pus from the prostate gland, loss of all symptoms and the failure to produce a recurrence. It is, of course, impossible to say whether or not any of these cases will eventually light up again.

It frequently happens when a new drug is introduced into medicine that it is abused by indiscriminate use before the full force of its power is recognized. Sulfanilamide is well on its way to produce much harm, as well as benefit, unless those who have to do with dispensing it adopt some measures for its control. The literature already is filled with reports of its side-effects. It was at first believed to be nontoxic, but with the great increase in its use, reports have shown that it should be used with caution. Since it will probably come to be used universally for the treatment of gonorrhea, one can readily visualize its uncontrolled abuse because of the advice one patient with gonorrhea passes to a fellow-sufferer, because of nation-wide publicity given the preparation under trade names, and because of the ease with which it can be purchased from any drug store counter without a prescription. Fancy the outlet through unethical pharmacies of this very useful but hazardous drug to people having gonorrhea; the criticism of the medical profession if some one should suffer great physical harm and perhaps death as the result of the use of Sulfanilamide. The cyanosis of sulphemoglobinemia is in itself not alarming since it quickly disappears on discontinuing the drug. However, if the total hemoglobin in a case of sulphemoglobinemia should fall below 30 per cent, the situation might prove serious. This condition in an uncontrolled patient will probably not be recognized by the patient and his illness most likely will be blamed for his ill-feeling, rather than the medicine which he is taking for it. If he then continues to use it the hemoglobin will be further reduced. It has been reported that during the administration of Sulfanilamide, magnesium sulphate by mouth or even wet dressings may predispose to sulphemoglobinemia.

SUMMARY

The use of Sulfanilamide in gonorrhea gives promise of being the first satisfactory treatment for that disease. Its effect is rapid when effective, and it has been successful in producing at least a clinical recovery in 90 per cent of our test series of 100 cases. It would seem that it is effective in inhibiting the complications of gonorrhea as well, and it may lend itself to the actual treatment of its complications and sequellae.

In our second series which was begun on May 1, 1937, 1 case of arthritis of gonorrheal origin has shown astonishing improvement.

From our observation the result of the treatment is almost predictable by the degree of disagreeable effects produced by the drug.

It is well to advise the patient against the use of magnesium sulphate during treatment.

The uncontrolled use of the drug in gonorrhea is associated with great hazard. Because of the wide publicity given it in newspapers and periodicals in connection with streptococcus infections, the various trade names are quickly recognized on the prescription. It can be bought indiscriminately at any pharmacy and used without control. Until such a time when proper steps shall have been taken to protect the public from its harmful effects it rests with the medical profession to bend every effort to assume that duty. This can be accomplished by placing on the prescription the words "Do not refill." The use of Sulfanilamide in our cases may have been continued somewhat longer than was necessary. This was because we did not have the experience to know when to consider the case terminated.

CHANGES IN THE THERAPY OF PEPTIC ULCER*

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Because peptic ulcer is a chronically recurring disease, etiologically not understood and with symptoms temporarily alleviated by many forms of therapy, the treatment of the disease has a rapidly changing pattern of both medical and surgical therapy which often follows a vogue. The popularity of one form of treatment, for example, may arise in the convenience of administering or prescribing a particular drug; while that of another is based on the recent report of an enthusiastic investigator or operator who has not checked his results by careful and prolonged clinical trial. Or again, a drug house resounds the virtues of a new product and a wave of credulity spreads over the profession, that here at last is the desired form of therapy.

The variegated pattern of medical therapy may be illustrated by recalling the 5 recommended diets described by Sippy, Lenhart, Warren-Coleman, Smith and Bassler with basic theories ranging from keeping the stomach relatively empty to partially filled with food. Vitamins have been given in acid fruit juices, while alkalinization reduces the acid contents of the stomach. Mucin, chicken gizzards, and okra have been fed and everything from foreign protein to amino-acids, to the anti-anemic principle of the gastro-intestinal mucosa has been injected. Surgical therapy has varied from cutting out the ulcer to widening the pylorus, diverting the path of food and secretions, to entirely removing the ulcer-bearing area. The mere multiplicity of therapies betrays how little we understand the basic theory of treating peptic ulcer, yet the ultimate failure of some have contributed to our understanding of the disease, while the temporary success of all have demonstrated how well the symptoms may be temporarily relieved by suggestion.

Now unfortunately a rational therapy for peptic ulcer must still for the present at least be appraised by the trial and error method until such times as the pathological entity can be exactly reproduced in the experimental animal. But because of the very chronicity of the disease this appraisal should always be evaluated by long continued follow-up studies of the results. Conversely, an immediate success should not be popularized. Vogues tend to obscure the fundamental knowledge accumulated from experience. It is, therefore, the purpose of this discussion to indicate the trend of surgical and medical thought in the therapy of peptic ulcer as obtained from follow-up studies, and against this background to evaluate recent developments in treatment.

Let us first consider the therapy of perforated peptic ulcer. Analyses of many cases have shown the following facts:

1. The age of the patient suffering a perforation is older than usually quoted. The majority are over 40 years of age and in a high percentage of cases perforation occurs in individuals with previous symptoms of peptic ulcer. When the history was taken after operation, 88 per cent in one series gave a history of ulcer of many weeks' duration. Therefore, if the disease were treated earlier, some perforations could be prevented. A corollary is that perforation occurs as a com-

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* Read before the Society, February 10, 1937.

plication of chronic peptic ulcer and must be guarded against.

2. The mortality from perforation is still too high, varying from 4.7 to 48 per cent with an average figure of about 25 per cent, and for the following reasons: (a) The laity is not sufficiently well informed to seek immediate medical care for intense epigastric pain preceded by indigestion. All patients under medical care for ulcer of the stomach should be instructed to present themselves at once if sharp pain or vomiting occurs; (b) surgical procedures are performed to remedy the ulcer also, rather than to treat the emergency alone. In skilled hands and in carefully selected early cases the construction of a gastro-enterostomy in a young individual does not lead to a higher mortality, as the statistics show, but the procedure is of questionable benefit, and its construction sets a bad precedent for additional operative therapy by unskilled hands in the face of impending peritonitis. In a recent follow-up study, Sullivan and I investigated the presence of pyloric obstruction after plication of perforated ulcers directly over the pylorus when a gastro-enterostomy was and was not constructed. Pyloric obstruction already present or feared as the result of the plication is the reason for constructing the gastro-enterostomy. Of 10 with gastro-enterostomies, 3 had a patent functioning pylorus without symptoms, 2 developed marginal ulcers at the new stroma, and 2 others had a subsequent recurrence of ulcer symptoms. Of 9 with plication alone none developed obstruction; 1 had a gastrectomy later for hemorrhage, and 1 still had symptoms of ulcer. Thus the presence of perforated ulcer directly at the pylorus does not necessarily mean that obstruction is present or will develop, the complication of marginal ulcer becomes an additional possibility, and the gastro-enterostomy constructed in the presence of a perforation does not give a higher percentage of cures than with plication alone. Gastro-enterostomy should only be reserved for the exceptional case of perforated peptic ulcer and not constructed because the patient is young, the perforation is recent, or necessarily because the ulcer is near the pylorus; (c) deaths from postoperative pneumonia are more frequent than realized, 25 per cent, and cognizance of this fact suggests an approach for a reduction in mortality.

3. Perforation of a peptic ulcer is not a blessing in disguise; the patient still has an ulcer and should be treated accordingly. Six of 45 surviving perforated cases treated at New Haven Hospital had to have second operations, and only 25 per cent of these were symptom-free without diet at the end of 3 years. In hospitals, however, it is generally the rule after operation to step up the diet to "regular" during the convalescence while as a matter of fact the patient should be discharged on a strict ulcer diet to the medical clinic for continued treatment. Gilmour and Saint have shown that if recurrences are to happen they usually take place within the first 2 years after operation. Dietary regulation should, therefore, be continued for at least this length of time.

TREND OF SURGERY FOR CHRONIC ULCERS

The trend of surgical therapy for chronic peptic ulcers is toward a reduction in the number of cases operated and toward more radical procedures when surgery is attempted. Let us compare, for example, 2 5-year periods of experience in surgery for chronic peptic ulcer at New Haven Hospital, the years 1923 through 1927, and 1930 through 1934. The figures for this clinic are not exceptional, but simply provide a ready analysis and concrete evidence of trend. There were 53 operations for chronic ulcer in the first period, and only one half that number or 23 in the second, although the number of cases treated both medically and surgically increased 2½ times in the last 5 years. In the first period, 9 per cent had gastrectomies, while in the last 5 years 48 per cent had them. In the first 5 years 3.6 per cent were second operations, while in the last 5 years 22 per cent were second operations, and mostly on patients with previous gastro-enterostomies. Fifteen per cent of those originally operated on in the first 5 years when gastro-enterostomies and pyloroplasties were still in vogue had to have second operations, but in spite of the fact that at least half the cases in the second 5 years have gone 3 years since the original operation, no secondary procedures have been necessary. The figures for the second 5 years indicate that when the operative procedures for peptic ulcer are carefully planned the necessity for second operations can be minimized and unnecessary deaths avoided. The total mortality for all surgical therapy of chronic peptic ulcer was 15 per cent in the first 5-year period and 4.4 per cent in the second in spite of the higher incidence of gastrectomies in the latter. There are many reasons for the reduction in mortality in the second period, but the exorbitant 15 per cent of the first can be explained by one essential fact. The first period was the time when surgical treatment was the vogue and the pyloroplasty, sleeve resection, and the gastro-enterostomy were supposedly the complete answers for the cure of peptic ulcer.

FOLLOW-UP STUDIES

The trend of follow-up studies would indicate that the gastrectomy at present at least seems to be the more logical therapy when surgery of peptic ulcer is to be entertained, and that the gastro-enterostomy should only be used when there is definite evidence of organic pyloric obstruction. Follow-up studies on 34 cases of gastro-enterostomy by Sullivan and me illustrate the increasing incidence of poor results when gastro-enterostomy is performed for indications other than obstruction. In these cases gastro-enterostomy was the first and only operative procedure and the follow-up studies were adequate. In 19, in which the indication for gastro-enterostomy was obstruction, there were 21 per cent poor results. Balfour, in a series of 600 gastro-enterostomies, reports 21 per cent poor results. However, in 7 cases done for other reasons, such as hemorrhage or complete failure of medical treatment, there were 28 per cent poor results, and in 8 cases in which there were no adequate reasons for doing the operation, there were 37 per cent poor results. The figures indicate that gastro-enterostomy is not as adequate surgical therapy for the treatment of peptic ulcer in general, as first believed, but that it is more nearly so when performed for peptic ulcer plus obstruction. Organic obstruction must, however, be carefully differentiated from pyloric spasm by adequate medical treatment.

The rationale of the gastrectomy is to remove the entire ulcer-bearing area. Birge in this country and the German surgeons have for some time claimed superior results with the gastrectomy, but again final judgment of the efficacy of this procedure must await longer follow-up studies. Marginal ulcers can result after gastrectomy, and symptoms may persist, although both seem to be diminished in numbers in comparison with other operative procedures. The high mortality of gastrectomy is no longer a bête noir. With proper selection of cases and with careful preoperative and postoperative care the mortality can undoubtedly be reduced to the neighborhood of 5 per cent. The recent introduction of the Wangensteen apparatus has furnished an additional instrument to combat postoperative complications.

The question was asked a few years back, and not without reasonable facetiousness, "How large must the ulcer be before the surgeon is willing to resect half the stomach?" The thinking surgeon is now so humble about his operative results for surgical therapy of chronic peptic ulcer that at present he lays down very rigid rules for all surgical intervention. These are: (1) the presence of organic pyloric obstruction, (2) the failure of truly adequate medical care, and adequate must be underscored, and (3) repeated and intractable hemorrhages. It is to be noted that the size of the ulcer is no longer a criterion for operation, but symptoms. Once having determined that the symptoms are intractable, though, to anything but surgery, he does not hesitate to resect or exclude the ulcer-bearing area. Size and location are considered, however, when malignancy is suspected, and the surgical dictum now is that all immediate prepyloric defects on the lesser curvature are to be suspected cancer until proven otherwise. The combined efforts of roentgenologist and pathologist have correlated the high percentage of malignant lesions in this location and the appreciation of this viewpoint is an advance in our understanding of the ulcer problem. Moreover, the careful roentgenological follow-up of the change in size of the gastric defect as advised and routinely carried out by Sara Jordan at the Lahey Clinic is a noteworthy contribution to therapy, for it provides a sound method to differentiate the gastric neoplasm from the gastric ulcer.

A word must be said about the adequacy of follow-up studies because the method of assembling the data is so important in evaluating changes in therapy, and adequate conclusions cannot be drawn from all so-called follow-up studies, especially those done by mail. One clinic, for example, reports only 1 per cent marginal ulcer after gastro-enterostomy while another reports 36 per cent, and other discrepancies not so obvious arise in some of the common errors of interpretation. In a group of 91 operations for chronic ulcer in New Haven Hospital, for example, there were 29 per cent poor results for all procedures and a total mortality of 12.1 per cent over a 10-year period. Actually the poor results are 41 per cent when one includes the fatalities, and even this figure is not adequate, since 13 per cent of the cases studied could not be traced. If these cases all did poorly the results reach the staggering figure of 59 per cent and the figure would be correspondingly lowered if these patients were all doing nicely. Moreover, when 100 per cent of patients return to a follow-up clinic the classification of the patient into "good" and "poor" results is often difficult. A patient who subsequent to operation has continued to have typical ulcer symptoms in the spring and fall each year must be classed as having a poor result, even though the patient is no worse. On the other hand, the patient who has occasional short attacks of gastric distress following certain specific foods must be classed as having a good result if he no longer suffers from his old ulcer symptoms. The necessity for frequent personal follow-up studies is easily illustrated. One patient returned to the gastro-intestinal clinic twice in the 2 years following his operation with definite recurrence of ulcer symptoms. He was placed on a careful medical régime and thereafter remained symptom-free. Five years later when he returned for check-up for the purpose of another study he stated that his operation had cured him and that he had never had any recurrence. Except for the record he would have been considered a shining example of a "cure" by surgical means.

RESULTS OF SURGICAL THERAPY AS SEEN IN G. I. CLINIC

It is not so many years ago, the late 1920's to be more exact, that the treatment of ulcer was definitely divided into two categories, medical and surgical, and there was considerable acrimonious debate between the two schools, one believing that nearly all cases of ulcer should be treated surgically, while the other felt that surgery should only be resorted to in emergencies. A good deal of the contempt of one group for the others originated in the fact that the internist saw only the surgeon's failures and the surgeon only the medical failures.

In New Haven Hospital, for example, of 91 patients operated upon for chronic ulcer, all but 29 per cent in the surgical follow-up study had good results, as already mentioned. But now let us compare these results with the picture received of surgical end results in general as seen by Sullivan in the gastro-intestinal clinic in the department of medicine. Patients usually seek the clinic because of the return of symptoms. Of 30 patients coming to the gastro-intestinal clinic with a history of operation for chronic gastric ulcer, 70 per cent had definite recurrence of ulcer symptoms after the first operation. Some of these were completely relieved of symptoms subsequently by gastrectomy, but many have had multiple operations without relief. Seven patients have had 2 operations, 1 had 3 operations, and 1 had 4 operations. The results of gastro-enterostomy were especially poor. Of

19 who had gastro-enterostomies as the first operation, 15 had had recurrences and 5 of these have had marginal ulcers. Here, then, in the same hospital there are two ways of viewing the end results of surgical treatment. In the surgical follow-up clinic only 29 per cent of the patients had poor results, yet in the medical gastro-intestinal clinic 70 per cent had poor results from surgery. The obvious answer is that the patients with good results do not seek the gastro-intestinal clinic, and the relatively low surgical percentage was influenced by an additional factor. Many of the poor results will not come back to the follow-up clinic of the surgical clinic where the operation was performed. This is borne out by the fact that many of the second operations performed on the surgical service had their first operation elsewhere. Of the 30 cases seen in the gastro-intestinal clinic, 14 had had their operations elsewhere and 100 per cent of them had had recurrences; and of 16 cases who received their first operation at the New Haven Hospital only 7 or 43.7 per cent had recurrences. Undoubtedly, many of the cases which could be traced in the surgical follow-up have had or will need subsequent operations and the patients will go elsewhere.

Adequate appraisals of end results could be obtained and the patients would receive better care anyway, if all patients were discharged from the surgical service after operation on a strict ulcer diet and referred to the gastro-intestinal clinic as still having an ulcer requiring medical care. In other words, when it is realized that peptic ulcer is a chronically recurring disease and that in spite of operation symptoms will recur in some individuals, a great advance will be made in the therapy of peptic ulcer. Then we will no longer try to distinguish between surgical and medical care but treat the patient medically throughout, with the operation constituting only the correction of a mechanical fault and not the cure of the disease. Considerable pride will have to be swallowed to do this, but we are gradually approaching such a viewpoint which is similar to that found in the management of other chronic diseases such as tuberculosis and diabetes.

Adequate Medical Care

Considerable has been said about adequate medical care and it is therefore fitting to discuss medical therapy at this time.

Adequate medical care can best be illustrated by indicating the fundamental aims sought for rather than by describing a particular diet or régime. The basic requirement is rest, and rest for the stomach means freedom from the corrosive effect of gastric juice rather than rest from peristaltic activity. The empty stomach has peristalsis and hunger contractions, but peristalsis is not markedly increased by a small amount of food, hunger contractions do not occur, pepsin is absorbed and the acid combined. On the other hand, over-distention, loss of tone, and stretching of the ulcer site result from filling the stomach with food and are absolutely to be avoided. Hence the advisability of frequent small feedings of bland foods which do not abrade the surface of the ulcer. Naturally the foods employed must not be secretagogues. In general, the diet should receive attention before alkalinization because the effects of powders are transitory. No rule of thumb can be laid down for the administration of powders, except that their use should not be abused and their contents should not be constipating. New antacids are produced every other month and advocated as superior for the therapy of ulcer. Consequently, they are frequently given before a dietary régime is established and the patient is allowed to fill his stomach to the point of distention 3 times a day. This is the favorite method of the faddist who follows vogues in medical therapy and who has forgotten the fundamental principle of rest.

Adequate medical care also requires complete body and mental rest. One is continuously amazed to find out how suddenly symptoms will disappear from the ambulatory obstinate case with hospitalization alone. Unfortunately, however, when patients are hospitalized the treatment is usually not continued sufficiently long after relief of symptoms to allow the ulcer to heal. Pain disappears from the leg ulcer with rest long before regeneration of tissue is complete and likewise the peptic ulcer once free of pain should continue under the régime for a sufficient length of time to allow complete healing of the defect. The same statement applies to increasing the diet too rapidly, for there is too often the tendency to regularize it as soon as pain disappears.

The presence of pylorospasm or organic obstruction should always be determined early, either by the use of the stomach tube, or better by X-ray, and treated early either by stomach washings or by the use of atropine. The cycle of spasm, pain, and more spasm is difficult to overcome. The use of atropine has always been opposed on an experimental basis, but clinically it works if given properly. When the dose is increased by 2 or 3 minims each time, as Sullivan has advocated, to the point of dryness of the mouth or slight blurring of vision and then reduced 2 or 3 minims below this point, the total amount required sometimes reaching 40 or 50 drops t. i. d., obstinate cases of spasm can be relieved. Novatropine has been marketed for the relief of pylorospasm because of its freedom from side effects, but the side effects really determine the dose required.

If no organic obstruction is present, continuous alkalinization by the nasal catheter should be tried for the obstinate case before surgery is contemplated. Gastritis should always be diagnosed either by the gastroscope or by X-ray and treated by stomach lavage. The patient should stop smoking and foci of infection should be eliminated. In fact, adequate medical care requires that every conservative means of therapy be exhausted before surgery is undertaken when there is no definite organic obstruction.

Because of the recurring nature of the peptic ulcer, a rational medical therapy now tries to prevent attacks, some of which happen with clock-like regularity. The patient should be instructed of the possibility of these recurrences, and before the fall or spring cycle begins the intensive régime which cures the attack after it is full-blown should be started. With colds, sore throats, and infections which frequently precipitate an attack, he should take to bed. It is my opinion that considerably more can be done with prevention and with the education of the patient than has already been accomplished.

Adequate medical care does not include injection therapy, unless the injections, for the present at least, are given for psychotherapy. Flood and Mullins have shown that sterile water has the same transitory effect on relieving the symptoms of chronic peptic ulcer as the injection of histidine. One cannot say, however, that an injection preparation will never be successful for the treatment of ulcer, but again if a particular one is to prove its worth, the drug should be given prolonged clinical trial and not popularized. Flood's work should be read by all those interested in the injection treatment of ulcers because every year a new injection preparation is advocated.

EVALUATION OF THERAPY FROM EXPERIMENTAL DATA

The statement was made in the introduction that because the disease entity has not been produced in the experimental animal changes in the therapy of peptic ulcer had to be proven by the trial and error method substantiated by a prolonged adequate follow-up. Many undoubtedly thought that this was a misstatement because surgical duodenal drainage will produce an ulcer experimentally. However, no one knows how this ulcer is produced by this operation or whether it is really chronic. Certainly we do know, though, that the complex chemical changes occurring in the animal after duodenal drainage are not found in the ulcer patient, and until such time as we understand which of these changes account for the formation of the ulcer it is useless to base a form of therapy on this experimental method. At first it was thought that the production of the ulcer by this method was the result of the deviation of alkaline protective juices from the ulcer-bearing area, but as a matter of fact the ulcer develops when a loss of gastric acidity is occurring. The animal suffers profound nutritional changes, loss of weight, cachexia, diarrhea, and a loss of serum protein almost to the level of nutritional edema. Loss of amino-acids as the explanation of the formation of the ulcer was a happy suggestion, but unfortunately histidine as now given does not work clinically, except for the initial success, and experimentally does not raise the serum nonprotein nitrogen nor protect as well as Aron and Weiss indicated. It is also questionable whether the ulcer produced by the method of surgical drainage is chronic. It is found 6 weeks after operation, but not after 3, and the dog dies before it is known whether the ulcer will heal. The same pathological picture can be produced at the end of 1 week by cutting a defect in the mucosa and exposing it to an abundance of acid and pepsin; but this lesion invariably heals in 14 to 16 days, as was shown by Flood and myself.

A fair percentage of peptic ulcers can be produced in dogs without surgical drainage by causing nutritional deficiencies alone, by feeding a diet low in protein and vitamin B. But to the contrary, most of the lesions produced in the stomach of the rat by vitamin deficiencies by Dalldorf and Kellogg, Pappenheimer, Carlson, and myself or by the injection of histamine by Büchner, Bürkle-de la Camp, Konjetsky, and others are not even anatomically equivalent to the peptic ulcer. They are multiple, involve the squamous epithelium also, and occur in hyperplastic glandular areas. It is significant, however, that the character of gastric epithelium can be influenced by the diet. But to read into these works a connection between vitamin therapy in the treatment of chronic peptic ulcer and the experimental data is unjustified. On the other hand, the question as to whether to give vitamins or not in the treatment of ulcer is easily answered. An adequate amount of vitamins does no harm and, therefore, can be given with impunity.

In conclusion, it should be emphasized again that all new forms of treatment of peptic ulcer should be viewed askance until time has proven their efficacy; and that we already have sufficient knowledge to take care of the majority of cases if this knowledge is adequately applied.

NOTE. Since this discussion was presented to the Medical Society of the District of Columbia, an article with similar conclusions has been published in the Journal, American Medical Association. See Sandweiss, D. J.: Comparative Results With Dietetic, Parenteral and Surgical Treatment in Peptic Ulcer. J. A. M. A., 1937, **108,** 700.

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THE ETIOLOGY OF PELLAGRA*

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Two hundred years ago, Casal, a Spanish physician, first described the clinical syndrome now recognized as pellagra. At the present time, the disease is regarded as practically world-wide in distribution, its effects being particularly prominent throughout the United States, India, Egypt, Spain, Italy, and Roumania. The thousands of pellagrous deaths recorded yearly in these sections of the world have naturally focused attention upon the causative factor or factors involved.

Three general etiological theories have been advanced by students of the disease. The earliest of these, the toxic theory, although still supported by some, has generally fallen into disrepute. The special feature underlying this view was the recognition of the high incidence of pellagra among persons whose diet was largely composed of maize. Associating this food substance with the pellagra of those people who used it, early writers concluded that the disease was the result of some harmful effect exerted by the material. Since it has been learned, however, that people may develop pellagra without maize as a part of their diet, and that they may recover from the disease even though they continue to ingest it, critical analysis has cast considerable doubt on the validity of the toxic theory.

The second general theory, that of infection, might be said to have been the earliest European view of the disease, but this was largely discarded at one time in favor of the maize theory of Lombroso. Rebirth of the idea took place in 1910, however, when Sambon vigorously maintained that pellagra was insect-borne, and probably transmitted by some species of gnat. There are those even now, both in this country and abroad, who hold that the disease is communicable. Reasons for such belief are numerous and many on first thought seem irrefutable. That the disease occurs in an environment of poor hygiene and sanitation, that it occurs in persons who have had contact with preëxisting cases, that there is a marked seasonal incidence, that it sometimes occurs in well-to-do and well-nourished persons is all good evidence to show that the disease is possibly of an infectious nature. Goldberger, in his monograph on the etiology of pellagra, however, has presented facts accounting for these questions, and consistent with the current popular conception of the cause.

The third general theory, and certainly the one which it seems fair to state occupies greatest favor at this time, is that of a dietary deficiency. The idea is not a recent one, in that Roussel, some 70 years ago first ascribed to diet a place of importance in the causation of the disease. Reliable evidence for this was slight, however, until the work of Goldberger and his co-workers. In a series of studies these observers first demonstrated that recurrences of pellagra may be prevented in susceptible persons by employing certain dietary measures; and they later showed that in some individuals the disease may be produced by allowing them only food that was previously found associated with its high incidence. Thus, by dietary manipulation alone, the disease was for the first time prevented and produced under controlled conditions.

Most students of nutrition having at this point accepted pellagra as a dietary deficiency disease, they directed attention to the specific material whose lack seemed responsible for its appearance. In 1912 Funk had included pellagra in a group of "deficiency diseases," curable by adding to the diet certain materials called "vitamins," an opinion which Voegtlin also thought worthy of consideration. As a result of studies upon Egyptian pellagra, Wilson maintained the essential deficiency to be that of protein, and in 1922 Goldberger and Tanner held that a lack of one or more combinations of amino-acids was responsible for the disease. The latter later discarded this view, however, and concluded that the protein factor, if concerned at all, was not the sole preventive or curative principle. As a result of these and other experiments, these authors designated the unknown principle as the P-P, or pellagra-preventive factor, naming among other foods yeast and lean meat as especially rich in its substance. Since yeast which up to this time was thought to contain only anti-neuritic vitamin B was also shown to be of pellagra-preventive value, the question of a relationship between old vitamin B and the new substance naturally arose. It had long been known that vitamin B contained both anti-neuritic and growth-promoting properties, and on first thought it seemed reasonable to suppose the pellagra-preventive substance to be a third. Further investigation showed this not to be true, however, and old vitamin B was re-named vitamin B_1, and the pellagra-preventive substance was called vitamin B_2 or vitamin G.

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It is well known that pellagra manifests itself principally in the skin, the gastro-intestinal tract, and the nervous system. Following the work of Goldberger and his co-workers, it seemed natural to conclude that the factor whose absence was responsible for one portion of the disease was also responsible for the entire syndrome. Because certain individual food substances such as yeast and lean meat contained material which resulted in the eventual disappearance of all manifestations of pellagra, that the disease might be the result of multiple deficiencies was lost sight of. Challenging the idea of single deficiency, Spies demonstrated improvement in the skin lesions of pellagrins maintained on a diet poor in vitamin G, although at the same time lesions of the gastro-intestinal tract became worse. It has, therefore, become apparent that the various components of the syndrome are in all likelihood not due to lack of a single chemical substance but probably involve a multiplicity of factors. Such is again suggested time after time as we see the variability in occurrence of abnormalities in the skin, gastro-intestinal tract, and nervous system in individual patients. In some the dermatitis may be severe and extensive with little or no abnormality of the gastro-intestinal tract, and then again the picture presented may be quite the opposite. Nervous system disorders may present themselves in combination with either the skin or digestive tract lesions or both, or then again may be the sole outstanding feature of the case. Fortunately, we know of certain materials which on proper administration will prove of benefit to pellagra in toto, but the chemical material responsible for the beneficial change in each single manifestation remains obscure. Within recent years investigative work has been successful in breaking down certain materials containing so-called vitamin G into different portions, but as yet isolation of the specific compound or compounds is to be done.

Pellagra may be said to develop in individual persons because of one of 3 reasons. There are, first, those people who actually eat normal quantities of food but are unable to retain it. There are, second, those who do not ingest normal quantities of food, either because it is not available or because they have lost their desire for it; and there are, third, those who both ingest and retain normal amounts of food but who for unknown reasons fail to assimilate or absorb it properly.

In the first group practically all may be said to be persons with organic disease of the gastro-intestinal tract. Carcinoma or other obstructive lesions of the esophagus, carcinoma of the stomach and benign but obstructive peptic ulcer have long been known to be potential predisposing causes of pellagra. Lesions of the lower bowel, such as cancer, tuberculosis, ulcerative colitis, and lymphogranuloma, when accompanied by marked diarrhea are sometimes seen complicated by the disease. The underlying reason that pellagra should develop in these people is obviously that of faulty retention of necessary food substances. In this connection it is interesting to note, however, the rarity with which pellagra appears in persons subjected to simple starvation. Why such should be true seems confusing until it is realized that pellagra preventive materials are probably stored in some of the bodily organs, and that the individual usually dies of the starvation before these substances become entirely depleted. In a like manner it seems probable that the reason we do not see pellagra more frequently then we do in persons with organic disease of the gastro-intestinal tract is because the patient dies of the primary disease before consumption of all the stored anti-pellagric materials has taken place.

By far the greatest number of pellagrins are those of the second group, who for various reasons do not ingest sufficient amounts of food containing pellagra-preventive substances. A small number of them may be called food faddists, who for reasons applicable only to their mental state eat types and quantities of food insufficient for their individual requirements. The influence of this group in making the disease an important public health problem is of course negligible. On the other hand, the tremendously high incidence of pellagra in endemic form among the poorer class throughout the South is of utmost importance. Why among these people such a high incidence of the disease should exist has been attributed to the paucity of suitable food materials available to them. The factors influencing this are naturally in the greatest sense economic, but it is now thought that should these people use the means at hand for procuring the proper types of food, the morbidity of the disease would be appreciably lowered. Recently the question has been raised as to proper interpretation of statistics which show that southern pellagra very definitely increased in the United States during the 1920's but has declined since (Reece). To some writers it has not seemed consistent that a disease, if entirely dependent upon nutrition, should increase in incidence during times of economic prosperity and decrease during a succeeding period of depression. This question has been answered by Sebrell, who suggests the effect exerted by the price of cotton upon the incidence of the disease in this country. He has maintained that when the price received for cotton is good the small southern farmer uses all available land for raising this staple, whereas, during depression years a part is given over to a vegetable garden resulting in an abundance of pellagra-preventive foods for the family. In connection with this it is interesting to note, however, that the depression in the price of cotton in 1914 was followed by an increase in the number of pellagra cases in the United States, whereas, a rise in the price during the following year was followed by a reduction (Goldberger). These inconsistencies seem to point out that more than one factor is responsible in the variability of the number of pellagra cases reported each year.

The relationship of so-called alcoholic pellagra seen in the North to the endemic pellagra seen in the South has long been debated. To some authors a relationship of dietary deficiency and chronic alcoholism has not seemed secure, and they have, therefore, regarded the disease seen in the alcoholic as possibly due to some toxic effect of the spiritous liquors. This idea, however, has been largely done away with, since Spies and DeWolf pointed out both that the effects of alcohol are only those of preventing the addict from eating, and that alcoholic pellagra is similar in its clinical characteristics to the endemic type. From these studies it has seemed reasonable to consider the two as practically identical, the endemic type occurring in persons who do not eat because of lack of food, and the alcoholic type occurring in persons who do not eat because of loss of desire for food.

The occurrence of pellagra among a number of persons whose nutritional history does not seem to warrant it is one of the most influential factors in causing some disbelief in the dietary theory. Such thought seems to be more prevalent in the South than the North. There, one is told by doctors, nurses, social service workers, and others well up in the social scale, that they have had relatives or friends who have died of pellagra. The idea that these people were not able to obtain sufficient amounts and suitable qualities of food would, of course, be inconsistent with their economic status. That they had no organic disease of the gastro-intestinal tract could be concluded in that pellagra made its appearance independently of other symptoms. That they were not chronic alcoholics was vouched for. These stories, vague as they are, naturally serve as a stimulation to one's skepticism of the dietary theory.

While studying endemic pellagra in Alabama last spring, I had the opportunity of observing 3 patients who beautifully illustrated just such a state of affairs. Two of these were people of good intellect and well up in the social scale. Each told of recurrent attacks of pellagra for several years but insisted that their dietary intake had always been adequate until the glossitis of pellagra had made it too painful for him to eat. In other words, they had always taken a normal quantity and quality of food until after the onset of each individual attack of pellagra. When first seen all 3 had classical manifestations of the disease which promptly disappeared on administration of yeast and liver extract. While thus in remission they were hospitalized, and each was given a diet containing meat, eggs, milk, and green vegetables in quantities equal to, if not more than that taken by a normal person. It is needless to say that great care was employed to see that each patient took all the food allotted him. Within the space of a few weeks under such a régime, all 3 again had the glossitis and to a less extent the dermatitis of pellagra. These signs of the disease rapidly disappeared on again administering yeast and liver extract.

On first thought it would seem that the disease developing in these 3 persons while taking a known adequate diet would materially aid in refuting the dietary deficiency theory. It is of great importance, however, to note that each patient on two occasions was cured after the addition of yeast and liver extract to his dietary régime. Thus it seems that the whole matter specifically points out individual predisposition to pellagra. It suggests that these persons very likely have some form of intrinsic physiological disturbance which necessitates, for prevention of the disease, larger amounts of anti-pellagric material than is normally required. In a like manner this seems a fitting explanation in the case of those other persons whose disease, having appeared while taking an apparently normal amount of food, has caused so much skepticism of the dietary deficiency theory.

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THE BIOCHEMICAL PROCESSES OF THE NORMAL AND THE DISEASED KIDNEY

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The first theory of the secretion of urine appearing in the literature was formulated by Bowman in 1842. Bowman advanced the idea that water and inorganic salts are excreted through the glomerulus of the kidney nephron and the organic constituents of urine are excreted through the kidney tubule. Two years later Ludwig postulated that all of the constituents of the urine pass through the glomeruli and that concentration of urine takes place in the tubules by reabsorption of water. There was very little experimental evidence in favor of these theories at the time of their announcement. The Bowman theory was the outgrowth of morphological studies of the kidney and the Ludwig hypothesis came as an attempt to interpret physiological phenomena in terms of physical chemistry. These two theories are of great historical importance, however, because they became the basis of subsequent experimental attacks upon the problem of urine secretion.

The principal features of the modern theory of urine secretion were stated by Cushny in his celebrated monograph in 1917. There are two essential parts to the Cushny theory, which are: (1) Filtration of non-colloidal constituents through the membranes of the glomerulus in the same concentration as they exist in blood plasma; and (2) reabsorption of water and certain threshold substances as the glomerular filtrate passes through the tubules. The Cushny theory is a restatement of the Ludwig hypothesis with two important additions. Cushny postulated that there is reabsorption of other substances besides water in the tubules and that this reabsorption is a selective or physiological process. He introduced also the idea that differences in pressure have an important effect. In the arterial blood of the glomerular vessels there is a positive hydrostatic pressure which serves as the energy for the diffusion of substances through the glomerular membranes. In these vessels there is also a force opposing diffusion which is the osmotic pressure of the blood constituents. Normally the hydrostatic pressure of the blood is greater than the osmotic pressure, hence water and diffusible constituents are pushed through the walls of the glomerular vessels and the epithelium of the renal capsule into the lumen of the latter. Thus the osmotic resistance of the blood, which is equal to a pressure of about 30 mm. of mercury, must be overcome before filtration in the glomerulus occurs; if the blood pressure becomes less than 30 mm., urine is not secreted. In the tubules, according to Cushny, the transformation of glomerular filtrate into urine is entirely a process of reabsorption, there being no secretory activity on the part of the tubular cells. Reabsorption in the tubules is not due to a physical force like the positive hydrostatic pressure producing glomerular filtration. The origin of the energy for this mechanism is not known and the process is described as a vital or physiological activity of the tubular epithelium.

The most outstanding evidence in favor of the filtration-reabsorption theory of Cushny has been obtained by Richards and his associates at the University of Pennsylvania. With an exceedingly skilful technic Richards and coworkers were able to collect glomerular filtrate from the capsule of the renal corpuscle of the frog by means of a micro-pipette and by ultramicrochemical methods made comparative analyses of the constituents of this fluid and of the blood plasma and the urine. Richards found that the glomerular fluid contains no protein and has the same pH as blood plasma. He observed also that the concentrations of sugar, uric acid, creatinine, chlorides, phosphates, and the injected dyes, phenol red and indigo carmine, are the same in glomerular filtrate as in blood plasma. This appears to be indisputable evidence that the mechanism of urine secretion in the glomerulus is a simple filtration.

A comparison of the chemical composition of blood plasma and of urine will reveal that the constituents of urine are present in a much higher concentration than they exist in the blood. In a representative chemical analysis, the urinary concentration of urea is 60 times that found in blood; likewise, uric acid is 20 times, creatinine is 100 times, sulphates are 60 times, and phosphates are 30 times as concentrated in urine as in blood. The limitations of these data are that they do not show where in the kidney nephron the concentration takes place. The findings of Richards' laboratory have an unmistakable bearing upon this question. If concentration does not occur in the glomerulus, as Richards' work has beautifully shown, then it must take place in the tubules. Moreover, Richards found by chemical analysis of bladder urine collected at the same time as glomerular filtrate was taken that the bladder urine was much more concentrated than the glomerular filtrate, thus showing by further direct experimentation that concentration occurs in the tubules.

With the fact established that the tubule is the site of urine concentration, the nature of the tubular mechanism became the subject of intensive research. A number of investigators have demonstrated by histological methods the presence of injected dyes in the tubular cells, and failing to observe these dyes in the glomerulus, argued that this was evidence of direct secretion through the tubular epithelium. However, Richards, with his microchemical technic, demonstrated the presence of these dyes in glomerular filtrate, thus showing that these substances get into the tubules by diffusion through the glomerulus and that they may appear in the cells of the tubular epithelium by the reabsorption process.

Further evidence in favor of tubular secretion has been brought forth by Marshall from studies of comparative physiology. In the kidney of the toadfish and the goosefish there is no glomerulus. In these animals urine is secreted through a structure which corresponds to the proximal convoluted tubule of the mammalian kidney. Marshall found that the aglomerular kidney of these animals could secrete substances found in the urine of animals with kidneys containing glomeruli. He claims this is evidence showing the kidney tubule has secretory ability. It is somewhat hazardous, however, to argue that what occurs in the aglomerular kidney of a lower form of animals represents the process occurring in the more highly differentiated kidney of higher animals.

There is other evidence indicating that the tubular cells have secretory activity. Ammonia is present in blood and glomerular filtrate in very small amounts and there are much greater quantities of ammonia in the urine than can be accounted for if all the ammonia were removed from the blood which passes through the kidneys. In fact, most of the ammonia of the urine is produced in the kidneys. Therefore, it seems obvious that ammonia is secreted through the tubular cells. And hippuric acid, which is also formed in the kidneys, apparently reaches the urine through tubular activity. Thus the Cushny theory does not fit the facts regarding tubular activity, and it seems justifiable to assume that the kidney tubules have a secretory as well as a reabsorptive function.

Recently evidence has been obtained which indicates that urea is reabsorbed by the tubular epithelium. Van Slyke, Hiller and Miller found that the clearance of urea in dogs with explanted kidneys is less than that of creatinine, inulin, and sodium ferrocyanide. Since the evidence indicates that the latter substances are not reabsorbed and their clearances are believed to be optimum, the most likely explanation of the lower clearance of urea is that urea is reabsorbed by the tubules. According to Van Slyke's data, urea is reabsorbed in the dog to the extent of 43 per cent.

Reabsorption of water by the kidney tubules is influenced by the secretion of the posterior pituitary gland. The disease, diabetes insipidus, in which there is a marked water excretion, is due to a lesion in the posterior pituitary. Polyuria occurs when the posterior pituitary gland is surgically removed from an animal, and this condition is relieved by injection of posterior pituitary extract. Pitressin, a chemical principle isolated from the posterior pituitary, has an antidiuretic effect upon unanesthetized animals. The kidney is extremely sensitive to pitressin, the polyuria of diabetes insipidus being relieved for many hours by the administration of a single unit of this substance. The amount of antidiuretic hormone in the blood and urine is so small under normal conditions that it defies detection. However, Gilman and Goodman recently demonstrated the presence of antidiuretic hormone in the urine of rats, dogs, monkeys, and man, when the experimental subjects were dehydrated by water withdrawal or salt administration, the dehydration serving as a stimulus to the gland to produce increased amounts of hormone. It has thus been well demonstrated that water reabsorption by the tubules is subject to the control of an antidiuretic hormone secreted by the posterior pituitary.

In summary of the foregoing, the present conception of urine secretion is as follows: In the glomerulus a simple filtration of non-colloidal constituents of blood plasma occurs. There is a reabsorption of about 97 per cent of the water of glomerular filtrate in the tubules. For the secretion of one liter of urine, almost 100 liters of filtrate pass through the glomeruli. In the tubules there is also a reabsorption of sugar, chlorides, bicarbonate, bases, urea, and probably other constituents. The degree of reabsorption of these substances varies, hence the mechanism is selective. Reabsorption of water is the principal concentrating factor in the production of urine; however, some substances, such as ammonia and hippuric acid, appear to be added to the urine by the tubules. Concisely expressed, the modern conception is glomerular filtration, tubular reabsorption, and some tubular secretion.

Having made a résumé of the normal mechanism of urine secretion, I shall now discuss certain phases of the biochemistry of the diseased kidney. Albuminuria, edema, nitrogen retention, the blood electrolytes, nephritic acidosis, uremia, and hypercholesterolemia will receive attention.

1. ALBUMINURIA. This condition is due to changes in permeability of the kidney glomerulus. The endothelium of the capillaries and the renal capsular epithelium become permeable to the large molecules of serum albumin and serum globulin of the blood and these proteins pass into the capsule and are excreted through the tubules. Albuminuria may be augmented by detritus from the tubules, but most of the proteins of albuminuria originate from the blood, entering the nephron by way of the glomerulus.

The principal causes of albuminuria are asphyxia from impaired circulation in the kidneys and irritation from toxic substances. Clamping the renal artery for 30 seconds will cause the appearance of albumin in the urine. This is due to asphyxia. Albuminuria also arises from the congested kidney of heart disease, from severe exercise, and in severe general anemia. These are all instances of lowered permeability of the renal capsule due to asphyxia, or reduced oxygenation. In organic disease of the kidney in which there is impaired circulation, asphyxia is also an important factor. Chemical irritants, such as mercury, arsenic, lead, cantharides, and the toxins of infectious diseases also lower the permeability of the glomerular membranes to proteins, producing albuminuria.

2. EDEMA. In edema of nephritic origin there is a decrease in the proteins of the blood plasma due to the excretion of plasma proteins in the urine. Nephritic edema therefore accompanies those kidney lesions in which there is marked albuminuria. It occurs in the acute and subacute stages of glomerulonephritis and in nephrosis. It is most characteristic in nephrosis.

The existence of edema becomes clear when the physiology of water balance is understood. The blood plasma proteins maintain a regulatory influence upon the water balance of the tissue. Normally blood plasma contains 4 to 6 Gm. of albumin and 1.5 to 3 Gm. of globulin per 100 cc. In albuminuria there are heavy losses of albumin in the urine and some globulin is lost. The losses of albumin are much greater because the albumin molecule is smaller than the globulin molecule and diffuses more readily through the permeable glomerular membranes. The normal albumin: globulin ratio of 2 or 3 to 1 thus becomes reversed. When the total plasma proteins get below 5.5 Gm. per 100 cc., or the albumin becomes less than 2.5 Gm. per 100 cc., edema sets in. The edema is caused by a lowered osmotic pressure of the blood due to decreases in protein content. In osmosis, the flow of water through membranes is from the less concentrated to the more concentrated solution. A lowered concentration of proteins in the blood, therefore, results in a flow of water in the direction of the tissues. The blood does not have an effective osmotic pull upon the water in the tissues, consequently edema arises.

For a long time it was believed that retention of chlorides is an etiological factor in the production of edema. Reports upon studies of the chloride content of the blood have shown, however, that in patients with edema the blood chlorides may be normal, or high, or low. The opinion that is now held is that retention of chlorides from kidney insufficiency is not a causative factor in edema and that nephritic edema is due entirely to hypoproteinemia. It should be realized that, while there is no disability of the kidneys to excrete chlorides, restriction of chlorides in the diet is indicated in cases of edema. This is because, up to a certain extent, salt in the tissues favors retention of water. If salt is given to an edematous patient, it rapidly passes into the tissues and accentuates the retention of water. The accumulation of chlorides in the tissues does not arise from inability of the kidneys to excrete chlorides, and is rather a reflection of the affinity of the tissues for salt under the existing conditions.

3. Nitrogen Retention. From animal experimentation it has been found that about three fourths of the kidney tissue may be removed before nitrogen retention occurs. This is an indication of the extent of reserve kidney function. Nitrogen retention occurs in all stages of glomerulonephritis, being most marked in the acute and chronic stages. It is absent or slight in lipoid nephrosis and does not occur in nephrosclerosis until the renal blood flow is considerably reduced. The principal nitrogen retention products are urea, creatinine, uric acid and amino-acids. Normally urea constitutes about 50 per cent of the nonprotein nitrogen of the blood and 90 per cent of the nitrogen of the urine. When retention occurs, the blood ratio of urea to nonprotein nitrogen increases in proportion to the severity of the condition, reaching values of 75 to 80 per cent in advanced cases. Because of the quantitative prominence of urea as a nitrogenous waste product the determination of the blood urea and the urea clearance are used as measures of kidney function. Retention of urea does not occur until the urea clearance has become about 50 per cent of normal, hence the urea clearance test is our most sensitive method of determining the nitrogen excreting capacity of the kidneys.

Since the nitrogenous constituents of the urine are excreted by filtration through the glomeruli, nitrogen retention must be considered as due primarily to a glomerular lesion.

Conceivably nitrogen retention may arise either from a reduction in the volume of blood passing through the kidneys or from a decrease in the amount of nitrogen metabolites removed from the perfusing blood.

In studies upon dogs with explanted kidneys Van Slyke, Rhoads, Hiller, and Alving found that the urea clearance directly parallels the rate of renal blood flow. It was not affected by oxygen consumption or a 10-fold increase in the blood urea. These findings strongly suggest that the speed of blood perfusion through the kidneys is the main physiological factor determining nitrogen excretion.

Retarded renal blood flow also appears to be the principal cause of nitrogen retention in kidney diseases. In cases of "stasis kidney," due to heart failure, the blood urea may go as high as 40 mg. per 100 cc., and return to normal when the circulatory embarrassment has been relieved, showing that the rate of blood flow is a determining factor in the retention of nitrogen. In acute and subacute glomerulonephritis there is reduced blood flow because of the congestion due to the inflammatory processes. In chronic glomerulonephritis, there is circulatory impairment due to a decrease in the number of functioning glomeruli. The observations of Richards are of interest in this connection. Richards made the very significant discovery that only a part of the glomeruli of the normal frog's kidney are patent. Thus in a microscopic field he noted that some glomeruli had an active circulation; others showed only a part of the capillaries functioning; and some were completely bloodless. This observation gives an anatomical basis for the well-known clinical fact that the kidneys have a marked reserve functioning capacity. Normally there are about 2,000,000 nephrons in a single human kidney. In chronic glomerulonephritis glomeruli have been destroyed by the pathological processes and their tubules have atrophied. These changes result in a reduction of the number of functioning nephrons, thus bringing about a decrease in blood flow through the kidney, as a result of which nitrogen retention occurs.

Back pressure upon the glomerular filtrate due to obstructive lesions in the urinary tract might also produce nitrogen retention. In hydronephrosis and cases of heavy albuminuria where there is plugging of the tubules by protein casts, back pressure is probably a causative factor.

Nitrogen retention might also arise from a decrease in permeability of the glomerular capillaries. In those lesions with albuminuria this seems unlikely because there is a known increase in the permeability of the membranes to the plasma proteins, substances whose molecules are several hundred times as large as any of the nitrogen retention products. On the other hand, in lesions where there is marked sclerosis of the blood vessels, decreased permeability must be considered as a possible etiological factor.

Other possible causes of nitrogen retention are decreased blood pressure in the glomerular capillaries and increased reabsorption of nitrogen metabolites in the tubules. The former is unlikely, as an increased blood pressure is usually the case in nitrogen retention, possibly as a compensatory factor, and the latter seems improbable since nitrogen retention is not characteristic of the nephroses, lesions in which tubular disease is the most marked, unless the glomeruli also are involved.

4. Blood Electrolyte Imbalance in Kidney Disease.

(a) *Chlorides.* It is questionable whether there is a tendency toward retention of the chloride ion in any of the kidney lesions. On the other hand, hypochloremia often accompanies the terminal or uremic stages of nephritis, being especially characteristic of bichloride of mercury poisoning. In these cases the kidney has apparently lost its ability to conserve its salt supply. The vomiting which accompanies these conditions is also a cause of chloride depletion. Chloride restriction in the diet is obviously irrational in kidney lesions of this type.

(b) *Inorganic Phosphate.* An increase in inorganic phosphate of the blood is a sign of renal insufficiency. In general, it may be said that phosphate retention occurs in those kidney lesions in which nitrogen retention exists. Elevation of the blood phosphate in advanced nephritis has prognostic significance. The determination of the blood phosphate does not give any information that is not obtainable from the creatinine or urea estimation, however, hence it has not received clinical adoption.

(c) *Sulphates.* The inorganic sulphate content of the blood is increased in glomerulonephritis. According to Wakefield and Power the elevation of sulphates in the blood appears earlier in kidney disease than urea retention or diminution in phenolsulphonphthalein excretion. The determination of the sulphate content of blood serum has not been introduced into clinical use, however.

(d) *Total Base.* In advanced nephritis, there is failure in reabsorption of basic ions. This results in a decrease in total bases in the blood. The decrease is almost wholly at the expense of sodium, calcium being diminished but very slightly, and potassium and magnesium are practically unchanged.

5. Acidosis. Richards found that the pH of glomerular filtrate is the same as that of blood plasma. The production of an acid urine is due to reabsorption of basic ions by the tubules. The kidney's part in maintaining the acid-base balance is the filtration of both acid and basic ions through the glomeruli and the reabsorption of bases in the tubules. The kidneys also exercise a controlling effect upon the acidity of the urine by ammonia production.

Nephritic acidosis arises in advanced nephritis. It is associated with inflammatory, arteriosclerotic, or degenerative changes and is, therefore, not peculiar to any type of kidney lesion. It is definitely related to the severity of the renal impairment.

The acid-base equilibrium of the body is the resultant of the balance between acid and basic ions in the body tissues. An increase in acid ions or a decrease in basic ions will produce the condition known as acidosis. Both of these tendencies occur in the acidosis of nephritis. In advanced nephritis there is a retention of phosphates, sulphates, and unknown acid ions, due to the reduced glomerular function; there is also a decrease in the total bases of the blood because of failure of the tubular epithelium to reabsorb basic ions; the ability of the kidneys to produce ammonia is impaired and ammonia is an important factor in the neutralization of acids of normal or abnormal metabolism. The electrolyte pattern of the tissues is thus disturbed in favor of the acid factors, and acidosis is the result.

6. Uremia. The term uremia was first used by Bright who thought the marked elevation of the blood urea is the cause of this condition. Neither urea, nor any other known constituent of the blood nonprotein nitrogen, appears to be responsible for the production of uremia. Large doses of urea or uric acid or creatinine may be given a normal individual without producing symptoms of this condition. Also, high blood urea values not due to nephritis have been observed in patients who did not have uremic symptoms. Much distress may be due to acidosis, or dehydration, but other factors contribute more largely to the toxic state. It has been suggested that indican or other toxic products of bacterial action upon proteins in the alimentary tract may be retained and produce the toxicity. The causes of the profound toxemia in this condition are not understood at present.

7. Hypercholesterolemia. There is a characteristic increase in the cholesterol of the blood in all kidney lesions showing edema. Apparently the condition is not related to water retention. In hypercholesterolemia of nephritic origin the glomeruli become permeable to cholesterol and there is marked cholesterol excretion in the urine. There is more or less reabsorption of this metabolite by the tubules, which accounts for the tubular deposits of cholesterol. Hypercholesterolemia associated with kidney disease is probably a result of impaired lipid metabolism, due to extrarenal causes. But concerning this condition facts are lacking, and the relation of hypercholesterolemia to the kidney lesions exhibiting it is not understood.

Summary

1. Urine is normally formed by simple filtration through the glomeruli, selective reabsorption from the tubules, and some tubular secretion.

2. Albuminuria arises from increased permeability of the glomerulus to plasma proteins caused by asphyxia or toxic irritants.

3. Nephritic edema is the result of hypoproteinemia due to losses of blood proteins by urinary excretion.

4. Nitrogen retention is the result of glomerular dysfunction. Two apparent causes are reduced renal blood flow and back pressure upon the glomerular filtrate by obstructive lesions in the urinary tract.

5. The blood electrolyte pattern is distorted

in kidney disease. Glomerular lesions are characterized by retention of phosphates and sulphates. There is a failure in reabsorption of bases, principally sodium, when tubular damage exists.

Chlorides are retained by the tissues, but not by the kidneys, in edema of nephritic origin.

6. Nephritic acidosis arises from retention of acid ions, and failure of the kidney to reabsorb bases and to produce ammonia.

7. The toxic factors in uremia and the relationship of hypercholesterolemia to kidney lesions are poorly understood.

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The Treatment of Bright's Disease and Related Renal Infections.—In the management of the various forms of Bright's disease, with rare exceptions, we can neither attack the underlying etiologic causes nor treat the pathologic processes in any fundamental way. We deal mainly with individual symptoms and we attempt to maintain the proper physiologic balance of the body. In so doing, much can be done not only to enhance the comfort of the patient but also, in many instances, to ameliorate the course of the disease. . . .

Renal Failure. In some cases of chronic glomerulonephritis, of malignant hypertension and of chronic bilateral pyelonephritis, the functioning kidney tissue may be reduced to such a point that renal failure supervenes, and eventually uremia may occur. The stages in this process, which may take place fairly rapidly or very slowly, can be summarized as follows:

1. The kidney loses its power to concentrate the urine. More water must be excreted to wash out the solid waste products and, hence polyuria and nocturia occur.

2. A stage is reached when the nitrogenous substances of the blood cannot be maintained at a normal level even by this method, and nitrogen retention occurs. This may be rapidly progressive or remain comparatively stationary for weeks or months.

3. Certain conditions result which tend to produce acidosis and dehydration. (a) Inorganic acids, especially pbosphates and sulfates, can no longer be adequately excreted and pile up in the body. (b) Chlorides are swept out with the dilute urine, and as the kidney further loses its power to manufacture ammonia, more and more fixed base, particularly sodium, is lost with the chlorides. This is aggravated by deficient salt intake due to anorexia, nausea or loss through vomiting. In the final stages the power to excrete an acid urine is lost, and the last defence against acidosis is gone.

4. The blood calcium may become lowered which condition is probably secondary to the low plasma proteins and retention of phosphates.

5. Anemia of a greater or less degree may occur, primarily on account of a toxic depression of blood formation, although in many cases a deficient diet has contributed to its occurrence.

The treatment for renal failure is in many ways diametrically opposite from that for nephritis with edema. Since nitrogen retention and marked edema rarely occur together, the indications for therapy are not likely to conflict. The principles of treatment are as follows:

1. When nitrogen retention begins to occur, as judged by an elevated blood nonprotein nitrogen, the protein of the diet should be restricted. If this nitrogen retention is a slow process, there is no point in limiting the protein to less than the minimal nitrogen requirement of the individual,—probably about 40 to 60 grams,—as the patient will merely burn his own body protein.

2. Chlorides must be provided to take care of the loss in the urine. Ordinarily, 5 to 7 grams of salt added to what is normally present in a salt-poor diet will suffice. In patients who are vomiting, it should be supplied parenterally,

3. Fluids should be given by mouth or parenterally in sufficient quantity to ensure, if possible, an output of 2,000 cc. daily in order to carry out as much waste substance as possible.

4. In the severe cases with acidosis, small amounts of sodium bicarbonate (2 to 3 grams daily) may help. Caution should be exercised in the amount given, however, because of the inability of such patients to handle alkalis well. Alkalosis can be precipitated by an overdosage of sodium bicarbonate.

5. If the symptoms of tetany occur or the blood calcium is very low, small doses of calcium may be given.

6. Attempts to relieve the anemia by iron or liver extract are usually unavailing, unless the anemia has been caused by blood loss or by a deficient diet. Transfusions may give temporary improvement.

Such treatment will often contribute much to the comfort of the patient and may prolong his life. In the cases, unfortunately not common, where the renal failure occurs as an acute exacerbation of the disease or where it is precipitated by some extraneous cause, such as heart failure or an infection, improvement may occur, and the patient may regain a degree of health for a considerable length of time.

Summary. Various forms of Bright's disease are discussed in regard to etiology and treatment. These include: acute Bright's disease; urinary infections, both in the acute and end stages; and chronic Bright's disease in the latent stage, in the stage with renal edema and in the stage with renal failure (uremia).

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A PATHOLOGICAL CLASSIFICATION OF THE NEPHRITIDES

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Over a century has passed since Richard Bright first described a clinical entity characterized by edema, oliguria and albuminuria. This condition is known in many circles as Bright's disease, however, we "moderns" prefer to speak of it as nephritis. Since the early publications of this distinguished physician in 1827 a voluminous amount of clinical and experimental data has accumulated, yet strange to say we have added little to his classical clinical description of the disease. Our knowledge, however, regarding the morphological changes in the kidney as the result of injury has been greatly widened. This fact is due primarily to the extensive use of the microscope, the application of which is essential in the diagnosis of the nephritides. The gross appearance of the kidney in the different types of nephritis is exceedingly misleading and those who rely for diagnosis on this criterion alone are due sooner or later for a rude awakening. The reasons are that in reality we know very little regarding the physiology of the kidney. Obviously its main function is that of excretion, although the processes by which this is brought about remain a mystery. The functional activity of the kidney is most complex and exceedingly versatile. As pointed out by Richards, almost any substance taken into the body will be excreted by the kidney, and it performs this task without disturbing the normal concentration of the blood constituents. When a large quantity of saline solution is injected intravenously, it is immediately excreted by the normal kidney, yet the quantitative elements of the blood plasma remain unchanged. We do not know what cells are responsible for this selective activity in the normal nephron. Likewise we do not know where the fault lies in the injured nephron under conditions of nitrogen retention. It is obvious to those of us who work at the autopsy table, that functional changes precede the pathological, and that microscopic variations precede the gross. Macroscopic changes are always the last to appear, and in the late stages are manifested by granularity, fibrosis, pits and scars. Countless numbers of pathological processes may cause any one or all of the above changes. If we cannot determine therefore the cause of scarification in other organs and parts of the body by gross inspection alone, why then should we expect to do so with such a complicated structure as the kidney?

It would be remiss at this time not to mention the fact that the terms "nephropathies" and "nephritides" are not synonymous. The former refers to all types of renal disease, including malformations, calculi, neoplasms, and the like, while the latter consists solely of derangements resulting from inflammatory, vascular, and degenerative conditions. This group was originally described as Bright's disease, and is the phase I desire to discuss and classify on a pathological basis.

The need for an understandable classification of the nephritides is obvious, since they stand today next to heart disease as a cause of death in this country. Statistics compiled by the Metropolitan Life Insurance Company show that 200,000 people die of heart disease in the United States every year and that 1 out of every 5 of the population living at the age of 10 years will die a cardiac death. Granting the above figures to be reliable, we must then admit that the nephritides run a close second "as the Grim Reaper," for the two conditions rarely occur separately. The reserve power of the kidney, like that of the heart, is enormous, yet neither is inexhaustible. Cessation, therefore, of function in either case results in certain death. The only difference being in the tempo of the process.

Early investigators realized this fact and saw the need for a more comprehensive understanding of the nephritides. As a result we find not less than 6 different classifications of the Bright's disease entity which includes more than 40 variations. Is it any wonder that confusion rather than sound reasoning has impeded the advancement of our knowledge? Of the classifications mentioned that are in common use, some are based on clinical observations and others on misinterpreted pathological conceptions. The urgent need today is for a profound understanding of the fundamental principles of renal function and the associated variations in the normal structure of the kidney as a result of injury. In other words, we need to establish a practical classification based on the known physiology and pathology of the kidney. Should we attempt to comprehend the heart murmur of valvular deficiency, we must be able to visualize the pathology and mechanism of stenosis and regurgitation; likewise, if we are to understand renal dysfunction and its relation to disease, we must be able to visualize the pathology in the kidney brought about by disease. An ideal arrangement, therefore, is one basic classification founded on accurate pathological observation and one which can be correlated with the symptoms produced in the various phases of the nephritides. This arrangement has gradually been accomplished primarily through the work of Bell and is the one used in our service with gratifying results.

The anatomy and histology of the kidney are familiar to all and do not require extensive elaboration here. It may be well to mention, however, that the excretory function is effected by means of a series of individual functional units. Each consists of 3 separate parts, the arterial supply, the glomerulus, and the convoluted tubule. While these portions of the unit are anatomically separate they are functionally dependent upon each other, and an injury to any one of them will profoundly affect the others. The remaining connective tissue framework of the kidney has nothing to do with excretion and should not be considered as taking any part in nephritic changes in true Bright's disease except secondarily.

It has been estimated that each kidney consists of more than 2,000,000 of these individual excretory units; however, Richards has shown that only a small number of these function at a given time. This fact explains the patchy distribution of the embolic glomerular lesions, so frequently associated with vegetative endocarditis.

For the moment let us consider that each kidney instead of consisting of 2,000,000 units is composed of only 1. The blood enters as usual through the artery or first portion of the unit which leads directly to the glomerular tuft. This latter consists of minute capillaries lined with normal endothelium resting on a basement membrane. The outer cover is made up of epithelium which is continuous with that of the surrounding capsule of Bowman. This structure, the glomerulus, or second part of the excretory unit, permits the water, salts, the nitrogenous waste products to filter through, but is normally impermeable to the serum protein molecules. The glomerular urine after excretion passes to the convoluted tubule, or third portion of the unit, where water and certain salts are reabsorbed. The artery or first portion which enters the glomerulus is known as the afferent arteriole, while that which leaves the tuft is called the efferent arteriole. This latter continues around and partially supplies the convoluted tubules. With this brief description of the histology of the kidney it is only logical to assume that any vascular injury would not only affect the arteries per se, but the glomerular tuft and tubules as well. This is exactly what we find and is the reason why the various clinical entities are so difficult to separate.

Glomerulonephritis is an inflammation of the glomerulus, and like other inflammations will result in resolution, or complete necrosis, or will pass through a subacute to a chronic stage with healing and resultant obliteration. The latter alternative is the most common and constitutes our first subdivision of the nephritides. Thus we recognize acute, subacute, and chronic glomerulonephritis, or for clarity we may regard it, as suggested by Volhard, as simply glomerulonephritis first, second, and third, or terminal stage. In the first or acute stage, the kidney is congested, red, edematous, and may show petechial hemorrhages in the cortex. For this reason it is descriptively spoken of as the large red kidney, or the "flea bitten" kidney, if hemorrhagic. Microscopically the endothelium of the tuft proliferates, the capsular epithelium becomes thickened and red cells and leukocytes collect in the capsular space and pass out in the urine. Should the patient recover, as is usually the case, the process continues to the second or subacute stage. Here the red cells and leukocytes tend to disappear, but the endothelium of the tuft continues to proliferate, often to the extent of producing complete occlusions of the lumen which results in an avascular glomerulus (Bell). The capsular epithelium desquamates and fills the capsular space so as to form a crescent about the tuft. This is the so-called epithelial crescent so characteristic of the second or subacute stage. The kidney is still large and edematous, and this associated with its relative avascularity gives it a white appearance. Hence the name, large white kidney. The healing process once started, continues usually to the third, chronic or terminal stage. Under such conditions the glomerulus heals with fibrosis, and its tubule in turn degenerates. Fibrous tissue proliferates to replace these structures and eventually contracts. The remaining excretory units, assuming additional duties, hypertrophy even to adenomatous proportions and may project through the cortex. These projections, separated by the connective tissue replacement, result in a granular, secondarily contracted or small white kidney so frequently seen in chronic nephritis.

Glomerulonephritis is the only inflammatory division of the classification. The other two phases are purely degenerative and include the simple nephroses and the arteriosclerotic kidney.

The term nephrosis was introduced by Muller and adopted by Volhard and Fahr to indicate a degeneration of the tubule or third portion of the excretory unit. As the tubule derives its blood supply from the efferent glomerular artery it is easy to see how any vascular or glomerular lesion would produce secondary tubular lesions. That is exactly what we find histologically. Any number of diseases, therefore, with varied etiology may produce nephrosis. I need mention only the common etiologic agents such as bacterial toxins, jaundice, chemical poisons, amyloidosis, and eclampsia. These conditions have nothing in common except the absence of inflammatory changes, plus the presence of tubular degeneration. The term, according to Bell, is acceptable so long as it is understood that nephrosis, per se, does not refer to any particular kidney disease, but to a group of conditions characterized primarily by tubular degeneration. The gross appearance in simple nephrosis is little altered and not diagnostic.

Our third and last subdivision consists of the arteriosclerotic kidney which is always degenerative in origin and chronic in course. We recognize anatomically 3 types of renal arteries, that is to say, first, the large artery which enters at the hilus and arches around the pelvis and calices; second, the smaller arteries or intertubular rami of the medulla, and third, the arterioles which enter and leave the glomerular tuft.

As arteriosclerosis may affect independently any portion of the intrarenal vascular system, so do we recognize 3 resultant arteriosclerotic subdivisions of the nephritides. We refer to these collectively as the nephrosclerotic kidneys, and specifically as the arterial, arteriolar and arteriolo types of nephrosclerosis.

Arterial nephrosclerosis associated with generalized arteriosclerosis of the aged is often called the senile kidney. Large areas of kidney structure atropy through loss of blood supply, while other portions undergo compensatory hypertrophy. As a result we find a markedly distorted, irregularly contracted organ with deep pits and projecting cortical nodules. While the senile kidney is obviously damaged, its function is little impaired, as a result of the compensatory mechanism, and no insufficiency results. Clifford Albutt speaks of it as a "starved but not a corrupt kidney, sufficient for the smaller life of the elderly man."

Arteriolar sclerosis is the most common type of nephrosclerosis and is present in almost all individuals after the age of 50. It may occur alone or in association with the arterial type, and even then it produces no dysfunction. The usual gross appearance of the kidney is that of granularity. The size is moderately diminished and the capsule is thickened and adherent. Upon removal, obvious decortication results and bleeding points are noted on the surface. The organ cuts with slightly increased resistance revealing practically normal-appearing cortical and medullary markings. There is also present an increase in the peripelvic fat which is a constant finding. The functional capacity of the kidney is not disturbed as a result of the above mentioned parenchymatous reserve although this is definitely diminished. If, however, arteriolar sclerosis is associated with sclerosis of the arterioles which supply the glomerular tuft, grave symptoms of hypertension and ultimate renal failure must ensue. The usual gross appearance in this combination is also that of granularity. In the later stages it becomes white and is then known as the primary contracted or again the small white kidney. This results from parenchymatous degeneration, associated with tubular hyperplasia, fibrosis, contraction and adenomatous cortical projections. The gross picture is identical with that of the secondary contracted kidney of chronic glomerulonephritis and it is only by means of a history and use of the microscope that the two entities can be accurately differentiated.

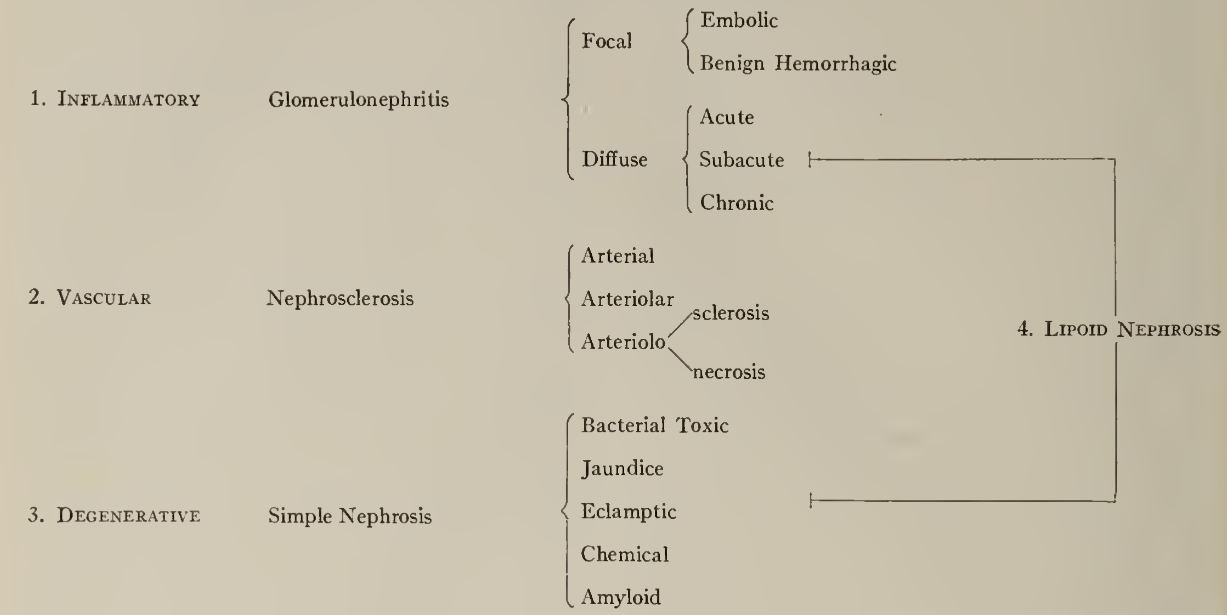
The third type of nephrosclerosis affects primarily the afferent arteriole of the glomerulus. This is the so-called hypertensive kidney, or the kidney of essential hypertension. All gradations of sclerosis are encountered, which vary from a slight thickening and hyalinization of the arteriole to a smudgy necrosis. The associated glomerular changes depend upon the degree and duration of the vascular damage. In the mild cases the glomerular tuft shows a diffuse hyalinization, while in the severe forms complete necrosis results. Anderson and Keith refer to these hypertensive cases as the benign type when the afferent arteriole and tuft show only hyalinization and the malignant type when they show necrosis.

It is practically impossible to predict the gross appearance of the hypertensive kidney at autopsy. In Bell's analysis of 420 cases of primary hypertension, he found 56 per cent showing smooth surfaces and 23 per cent with finely granular cortices. Only 15 per cent showed sufficient atrophy to warrant the term contracted kidney. Over 90 per cent, however, showed microscopic evidence of arteriolosclerosis which was often conspicuous in kidneys that showed no macroscopic changes. In the more or less acute types of malignant hypertension, associated with arteriolo necrosis, contraction is rarely found. In these cases the process has been too fast for atrophy to develop. The kidneys are often of normal size or may be somewhat enlarged. Their surfaces are smooth or finely granular and often covered with small hemorrhagic spots. They resemble in this respect the "flea bitten" kidneys of acute glomerulonephritis, but differ in that the hemorrhages in the former are petechial in character, while in the latter they are purpuric.

It would be amiss to stop here without saying a word about lipoid nephrosis. This term was introduced by Volhard and Fahr in 1914 as genuine nephrosis and later by Epstein as lipoid nephrosis. It occurs in young people and is characterized clinically by oliguria, extreme edema, and an inversion of the albumin-globulin ratio of the blood. There is also an associated hypercholesterolemia and red cells may appear in the urine. These investigators attribute it to a true tubular degeneration and classify it as a distinct entity. I have never seen a case on our necropsy service, which is not unusual, because such patients usually recover. The kidneys examined by these workers, however, are described as large and white, with yellowish streaks in the cortex, and they are, therefore, called the myelin kidneys of nephrosis. Yet this picture is exactly what we find grossly in the second stage of glomerulonephritis. Microscopically, one finds the tubules degenerated and hydropic and their cells filled with doubly refractive lipoid bodies which have been shown chemically to consist of cholesterol. The glomeruli are described as being almost normal in appearance. They may appear normal with ordinary stains, but they must be damaged, otherwise albumin would not be lost and salt retained. This is an example of functional changes preceding the pathological. Bell has shown by special stains that in every case of so-called nephrosis there is intracapillary proliferation of the glomerular endothelium, associated with a thickening of the basement membrane.

The symptoms of lipoid nephrosis are not unlike those of early subacute glomerulonephritis, and the gross and microscopic appearance of

THE NEPHRITIDES
A Pathological Classification



- 1. INFLAMMATORY — Glomerulonephritis
  - Focal
    - Embolic
    - Benign Hemorrhagic
  - Diffuse
    - Acute
    - Subacute
    - Chronic
- 2. VASCULAR — Nephrosclerosis
  - Arterial
  - Arteriolar
  - Arteriolo
    - sclerosis
    - necrosis
- 3. DEGENERATIVE — Simple Nephrosis
  - Bacterial Toxic
  - Jaundice
  - Eclamptic
  - Chemical
  - Amyloid
- 4. LIPOID NEPHROSIS

the kidney in the two conditions cannot be differentiated with accuracy. The only cases, according to Boyd, that escape critical analysis, are those in which the pathologist has not had an opportunity to examine the kidney. All cases observed by him following recovery from lipoid nephrosis eventually developed chronic glomerulonephritis and died a uremic death.

From the foregoing brief description of the clinical syndrome of lipoid nephrosis and the studies of Bell and Boyd on the corresponding pathology in the kidney, I feel justified in classifying lipoid nephrosis as a phase of subacute glomerulonephritis and not as a distinct entity.

In conclusion, permit me to summarize as follows:

1. The above classification is a pathological one based on characteristic changes in the functional excretory unit of the kidney in Bright's disease.

2. It consists of only 3 large subdivisions, the inflammatory, degenerative and arteriosclerotic with their respective subdivisions.

3. The symptoms associated with each of these phases of renal injury are fairly constant and characteristic.

4. The adoption and comprehension of this simple arrangement of kidney diseases should enable the clinician to better understand the pathological physiology of the kidney and also to visualize the renal changes therein and correlate them with the symptoms produced in nephritis.

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METHODS OF VENOUS PRESSURE DETERMINATION

Angelo M. May, A.B., and Marjorie M. Crittenden, B.S.*
Washington

The value of the determination of venous pressure in the diagnosis and prognosis of cardiac conditions has been well established by many. The work of Berghausen, Clark, Friedfield and Fishberg, Eyster, and Hussey may be mentioned. Kastlin and Machlachlan have shown the value of its determination in cases of pneumonia.

The main obstacle to its widespread clinical use has been the awkwardness and uncertainty of the methods of its determination. Gaertner was the first to measure venous pressure, which he did by the indirect method, i.e., raising the previously lowered hand to a height at which the superficial veins collapsed and reading the distance from the axilla to the hand as the venous pressure in centimeters of water. Robertson has called attention to this method in his paper in 1933.

In 1930 Taylor, Thomas and Schleiter described their direct method of venous pressure determination. Their apparatus consisted of a needle, rubber connection and glass tube into which the blood was allowed to run until it had risen to the venous pressure level.

Beck and Cushing, in 1934, published their method by which saline solution was allowed to flow into the vein until the column of the fluid in an open system became stationary. Their apparatus consisted of a funnel, glass tube, rubber connection and an 18-gauge needle. The venous pressure was measured in centimeters of water from the midaxillary line to the top of the stationary column of saline solution.

Griffith, Chamberlain and Kitchell also in 1934 described a method employing a 20-gauge needle and a 2 cc. syringe having a side arm to which a calibrated glass measuring tube is connected by rubber tubing the size of a 14 French catheter. The other end of the glass is connected to a reservoir filled with physiological salt solution. In this method the needle is inserted into a vein, the plunger of the syringe is drawn back allowing saline to run through the side arm into the syringe and thence into the vein. Next the reservoir is detached from the apparatus and the zero point of the calibrated tube is placed on a plane with the midaxillary line of the patient. This plane was arbitrarily selected as approximately the level of the right auricle in the supine position. The saline falls to the venous pressure level and stops. With this method the normal pressure readings have been found to vary from 40 to 120 mm. of water.

We propose 3 new methods of venous pressure determination, the first 2 working on the principle described by Beck and Cushing, and the last upon one yet not employed.

Murphy Drip Method

The apparatus consists of an 18-gauge needle, wide glass tube to which is connected a Murphy drip attachment and a reservoir (Fig. 1). The glass tube is allowed to fill by allowing the Murphy drip to flow. Then the clamp above the Murphy drip is closed and the column of saline solution is allowed to descend to the level of the venous pressure, measured in millimeters from the midaxillary line.

T-Attachment Method

The apparatus (Fig. 2) consists of an 18-gauge needle, needle adapter, and rubber tubing attached to a T tube, one arm of which is connected to a reservoir, and the other to a glass tube calibrated in millimeters. Three clamps are placed on the rubber tubing proximal to each arm of the T attachment. The vein is entered in the usual manner, and the blood in the needle is washed into the vein by opening the clamps on the needle and reservoir arms. Then the needle clamp is closed and the clamp on the calibrated tube arm is opened. This allows saline solution

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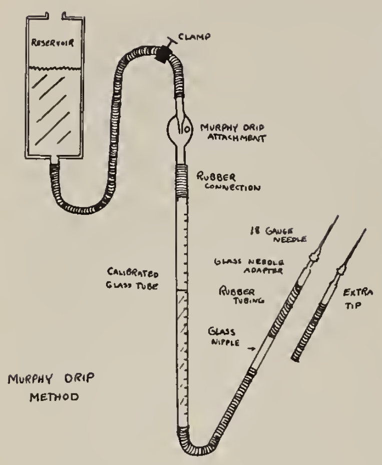
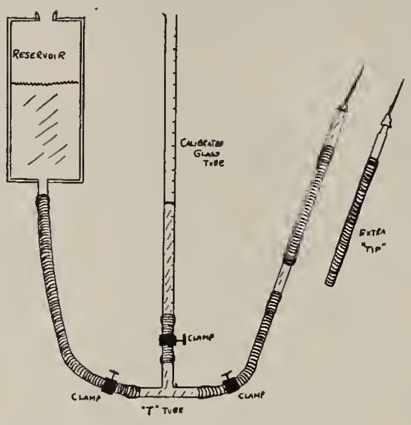
* Senior Medical Students, George Washington University School of Medicine.

- FIGURE 1 -


RESERVOIR
CLAMP
MURPHY DRIP ATTACHMENT
RUBBER CONNECTION
18 GAUGE NEEDLE
GLASS NEEDLE ADAPTER
CALIBRATED GLASS TUBE
RUBBER TUBING
EXTRA TIP
GLASS NIPPLE

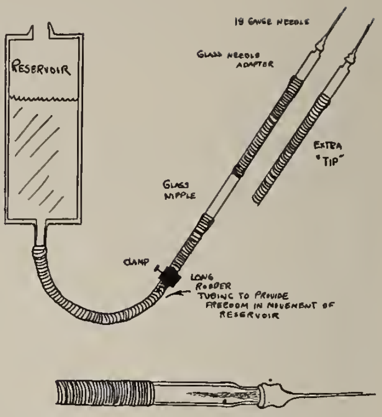
MURPHY DRIP METHOD

- FIGURE 2 -


RESERVOIR
CALIBRATED GLASS TUBE
EXTRA "TIP"
CLAMP
CLAMP
"T" TUBE
CLAMP

"T" TUBE METHOD

- FIGURE 3 -


RESERVOIR
19 GAUGE NEEDLE
GLASS NEEDLE ADAPTER
EXTRA "TIP"
GLASS NIPPLE
CLAMP
LONG RUBBER TUBING TO PROVIDE FREEDOM IN MOVEMENT OF RESERVOIR

SHOWING TIP WITH WISP OF BLOOD INDICATING END POINT

REGURGITATION METHOD

from the reservoir to fill the tube. The reservoir clamp is then closed and the needle clamp opened. The saline is allowed to flow from the tube into the vein until the venous pressure level is reached.

For both apparati extra "tips" consisting of a short piece of rubber tubing, a needle adapter, and an 18-gauge needle are provided so that successive venous pressure determinations on different patients may be made without sterilizing the whole apparatus anew, the "tips" merely being changed.

In these methods 3 advantages are prominent:

1. The needle may be left in the vein and several readings made, i.e., in inspiration, expiration, during intravenous administration of fluids.

2. The one apparatus can be used to determine several patients' pressures, interchanging the sterile "tips."

3. Proper time can be taken in the determination to make sure the reading is correct.

REGURGITATION METHOD

The third method possesses all these advantages and a fourth a simplicity of preparation and ease of operating. It consists merely of an ordinary intravenous set equipped with an 18-gauge needle. The needle is inserted into the vein and a few cc. of saline solution allowed to enter the vein. Then the reservoir is lowered slowly until a wisp of red-tinged fluid is seen to regurgitate into the glass needle adapter. This indicates the venous pressure level has been reached. The reservoir is held against a ruler with its zero mark at the midaxillary line, and the height of the top of the fluid in the reservoir is read. This height is the venous pressure in millimeters of water. The replaceable "tips" used in the previous apparati may also be employed here when successive readings on different patients are desired to be made.

The accuracy of the regurgitation method has been checked with the Murphy drip method, and in 20 cases the difference of end point of the fluid flowing into the vein and the regurgitation of the diluted blood was not found to exceed 10 mm. in any case, which is well within the range of incidental error in placing the ruler at the midaxillary line. The one precaution that must be taken is that the reservoir must be lowered very slowly when approaching the venous pressure level. It is sometimes advantageous to make 2 or 3 determinations, the last one with the idea of getting a very accurate reading by proceeding very slowly as the previously determined level is approached.

SUMMARY

Three new methods of venous pressure determination are described, the third being in the author's opinion the simplest and most applicable to every-day clinical use and requiring as apparatus only the ordinary venoclysis set employed routinely in hospitals.

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ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"Seasonal Variation in the Intensity of the Brain Reaction of the St. Louis Encephalitis in Mice and of Endemic Typhus in Guinea-pigs,"*† **R. D. Lillie, M.D.**, Surgeon, **C. Armstrong, M.D.**, and **R. E. Dyer, M.D.**, Senior Surgeons, and **J. G. Pasternack, M.D.**, Passed Assistant Surgeon, United States Public Health Service.

In the course of the encephalitis studies of Armstrong and Wooley, pathologic studies of the brains were made in a series of over 1,900 mice out of a much larger series inoculated with varying mixtures of virus and sera. As the work progressed, a disturbing decrease in the frequency of definitely positive reactions occurred. Analysis showed that this decrease was orderly and progressive, reaching a maximum in June and July, and followed by a sharp increase in August. When the percentages of moderate and marked reactions, and of all definite reactions, are charted by months, and the mean monthly temperature is charted inverted on the same chart, the 3 curves show a striking parallelism.

Separating the animals into 4 groups according to the approximate number of fatal doses of virus given and again charting by months showed the same seasonal variation in all of the 4 several groups, those receiving the lowest dosage showing the lowest proportion of definitely positive reactions, and those receiving approximately 1,000 times as much the highest.

A series of studies on the effect of environmental temperature on the development of the disease was made by Armstrong, and 128 brains taken from this series were studied pathologically. The 58 animals kept at 35°C. showed the lowest proportion of definitely positive reactions (50 per cent), 14 kept at about 10°C. showed 21 per cent slight and 79 per cent moderate reactions, 35 at room temperature (23°C.) showed 37 per cent moderate or marked reactions, and 46 per cent slight. The inocula and diet were identical in this series, and the various groups were run simultaneously.

Application of monthly grouping to the series of guinea-pigs with endemic typhus reported by Lillie and Dyer, revealed a similar seasonal variation in the intensity of the reactions. However, these animals were inoculated with various materials from various strains of virus taken over a period of several years, and some months were represented by quite inadequate numbers of animals.

Consequently, we determined to run a consecutive series over a full year, and to further test the temperature influence, part of the animals (289) were inoculated and carried through at the branch laboratory in Mobile, Alabama, by Dr. George D. Brigham, and the balance (226) here.

Charting the average numbers of lesions counted in a standard series of sections by months showed a high period from February to May, a low period from June to August, a September rise, and a second high period from October to January. In both places the curves of average numbers of lesions and the mean monthly temperature, charted inverted, showed a striking parallelism.

Incomplete experiments now in progress indicate that guinea-pigs maintained at about 33°C. show considerably lower average numbers of brain lesions than do those kept at room temperature or at about 16°C.

The present indications are that environmental temperature exerts a direct influence on the intensity of the pathologic reactions in the brain to these 2 viruses. The mechanism of this process is now under study, but as yet no results are available.

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* Presented at the joint meeting of the Washington Society of Pathologists and the Medical Society of the District of Columbia, February 24, 1937.

† From the National Institute of Health, Washington, D. C.

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TRICHINOSIS

FREQUENT FAILURE TO DIAGNOSE

Recent investigations have shown wide distribution of infestations with the Trichinella spiralis heretofore unrecognized. Dr. Maurice C. Hall, Professor of Zoology, United States Public Health Service, in "Studies in Trichinosis,"* states, "Between light infestations, producing zoological but not clinical trichinosis, and heavy infestations, producing severe clinical trichinosis, there is the unstudied no-man's land of infestations of intermediate degrees of all sorts, which infestations must produce atypical clinical trichinosis of unknown symptomatology." Here a picture of the situation is given which may well cause careful thought. The symptomatology varies widely according to anatomical areas involved, thus they may range from severe nervous manifestations to the simulation of a simple gastro-enteritis; cardiac disease pictures not infrequently are in evidence. To the diagnosis by biopsy, examination of stools for trichinae, the blood and cerebrospinal fluid for larvae have been added a skin test and a precipitin test. However, the latter tests have a disadvantage in that they are positive after a rather long time interval has elapsed from the initial infection. Further, it has been pointed out that more careful study is needed in "titration, standardization, preparation of antigen, and interpretation of reaction." When cardinal symptoms such as fever, marked eosinophilia or suborbital edema and myalgia are present one should know that the National Institute of Health will cooperate in making skin or precipitin tests. A startling statement is made to the effect that "1,778 cadavers in 24 hospitals in 11 places in the United States showed an incidence of 12.5 per cent of trichinae—not 1 case of 222 positive cases ever diagnosed at any time." The profession in Washington particularly should be aware of the work being done in this type of infestation as the incidence locally apparently is much higher than usually recognized. Physicians should freely accept the proffered assistance of the National Institute of Health to the end that cases of trichinosis will be more readily brought to light. A campaign for better animal husbandry, meat inspection and food preparation is patently suggested as a prophylactic measure of importance.

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* Pub. Health Rep., 1937, **52,** 539.

TRANSACTIONS OF THE SOCIETY

Stated Meeting, May 12 and 19, 1937

Result of election of officers and committee members:

To serve from July 1, 1937, to June 30, 1938:
  Thomas Edwin Neill, *President*
  Daniel Bruce Moffett, *First Vice President*
  Jacob Kotz, *Second Vice President*
  Coursen B. Conklin, *Secretary-Treasurer*
To serve from July 1, 1937, to June 30, 1939:
  Delegate, American Medical Association—Henry Cook Macatee
  Alternate, Arthur C. Christie
  Members, Compensation, Contract and Industrial Medicine Committee—
    Margaret M. Nicholson
    James N. Greear, Jr.
To serve from July 1, 1937, to June 30, 1940:
  Members, Executive Committee—
    William Mercer Sprigg
    Daniel L. Borden
    Henry R. Schreiber

The following were duly elected to membership, upon recommendation of the Committee of Censors:

Active Members

William Henry Beard, 3701 R Street, N.W.
Andrew Joseph Betz, 800 Butternut Street, N.W.

Sterling Bockoven, 1752 Massachusetts Avenue, N.W.
Warren Bernard Burch, 212 Maryland Avenue, N.E.
Catherine Welch Johnson, 2904 Nichols Avenue, S.E.
Ann Patrick Kent, 2112 Wyoming Avenue, N.W.
Benjamin Paul Lafsky, 5421 Seventh Street, N.W.
William Cornelius Lambert, 1526 Trinidad Avenue, N.E.
Arthur Harry Lewis, 1714 Rhode Island Avenue, N.W.
Paul Abraham Lichtman, 1835 Eye Street, N.W.
James Morgan Loftus, 1359 Monroe Street, N.W.
Barton Winters Richwine, 1835 Eye Street, N.W.
John Arthur Simpson, 721 Monroe Street, N.E.
Albert McElroy Wheeler, 1463 Rhode Island Avenue, N.W.

Associate Members

Alonzo Ray Dawson, Arlington, Va.
Robert Henry Detwiler, Arlington, Va.
B. Edwin Erikson, D.D.S., 3726 Connecticut Avenue, N.W.
Frederick Walters Norris, 1704 D Street, N.E.

Applicants for membership to be voted on in November, 1937:

For Active Membership

Walter Kavanagh Angevine, Georgetown University—1929
Edward Ballard Broocks, University of Virginia—1916
Peter Paul Brue, Georgetown University—1935
Ralph Cohen, University of Maryland—1915
Robert Francis Costello, Georgetown University—1932
Max Ellis Feldman, Medical College of Virgina—1932
Enoch Raymond Fenton, Medical College of Virginia—1930
Eugene Antonio Forcione, University of Rome—1922
Oscar Hugh Fulcher, University of Virginia—1926
Aaron Harry Gerber, George Washington University—1934
Reuben Goodman, Syracuse University—1930
John Estes Hanby, University of Pennsylvania—1932
Richard Stephen Hulburt, Georgetown University—1931
Alan Frank Kreglow, Medical College of Virginia—1934
Alexander Camillo Leonardo, George Washington University —1929
Charles Edwin McNamara, Georgetown University—1931

For Associate Membership

Thomas Henry Quill, Georgetown University—1933

By action of the Society, taken on the evening of May 12, 1937, Dr. Samuel M. Becker was dropped from the membership rolls of the Society. This was pursuant to recommendation received from the Executive Committee and the Compensation, Contract and Industrial Medicine Committee.

ACTIVITIES OF SECTIONS

Section on Internal Medicine

The result of election of officers for the year 1937–1938, is as follows:

R. Lomax Wells, *Chairman*
Walter K. Myers, *Vice Chairman*
Fred A. J. Geier, *Secretary-Treasurer*

REPORT OF COMMITTEE ON GROUP HOSPITALIZATION, INC.

The third annual meeting of the officers, trustees and Board of Directors of Group Hospitalization, Inc., was held February 9, 1937, in Room I, United States Chamber of Commerce Building at 8 P.M. A brief accounting of the activities of the organization throughout the fiscal year, January 1, 1936, to December 31, 1936, was made. This included a careful financial report submitted by the Director, which had been approved by a trustworthy Certified Public Accountant. This report showed a cash balance, December 31, 1935, of approximately $36,000.00. On December 31, 1936, the cash balance on hand was approximately $122,000.00. During the period of the report, January through December, 1936, over 3,000 individual cases have received hospitalization benefits. Subscribing members as of December 31, 1935, were 17,468, while on December 31, 1936, they totaled 34,485. These subscribers represented groups from a very wide variety of local business offices, Federal agencies, business concerns, etc. The report clearly indicated to the members of the committee present that Group Hospitalization, Inc., has proven itself a definite success from every angle. It has provided proper and satisfactory hospitalization among a large number of the wage-earning class. The organization has been conducted along unusually high standards as to ethics, personnel, etc. The business details have been apparently handled intelligently and efficiently and economically. Your Committee, therefore, strongly indorses this organization and speaks for the continued support and coöperation of members of the Medical Society in its activities.

Respectfully submitted,
Wm. M. Ballinger, M.D.,
For the Committee on Group Hospitalization, Inc.

Committee personnel:

William M. Ballinger
Joseph B. Bogan
Caryl Burbank
Tomas Cajigas
William W. Chase
Arthur C. Christie
C. W. Culver
William T. Gill, Jr.
R. Arthur Hooe
LeRoy W. Hyde
Richard A. Kearny
Leon A. Martel
H. J. Russell McNitt
Albert E. Pagan
Philip O. Pelland
Alec A. Preece
Frederick A. Reuter
J. R. Verbrycke, Jr.

MEDICAL-DENTAL SERVICE BUREAU, INC.

Annual Report to the Coöperating Societies, Submitted March 31, 1937

The Medical-Dental Service Bureau, Inc., of Washington, D. C., has finished its second complete year, and the Executive Director submits this report with a certain amount of pride, although he does not in any way wish to take credit for what has been accomplished by the Bureau. A full measure of credit should be given to the following: Mr. Ross Garrett, who directed the activities of the Bureau through the organization and experimental period; the hospitals and doctors who have coöperated with the Bureau; past and present employees who have worked long and diligently; and the Board of Directors who have contributed so much toward the success of this enterprise.

The following figures demonstrate the activities of the Medical-Dental Service Bureau since its inception, March 1, 1935, to March 31, 1937:

411 Physicians have used the Bureau.
125 Dentists have used the Bureau.
2,467 Applications have been received.
2,076 Applications have been accepted.
356 Applications were referred to the Central Admitting Bureau for Hospitals, the Board of Public Welfare, or rejected or not completed for various reasons.
8,028 Accounts were set up and collections made thereon for the Central Admitting Bureau for Hospitals. These accounts represent sums to be paid by semi-indigent patients as that portion of the cost of their hospitalization which is within their ability to pay.

	Business	*Collections*
	For the Two Years	
Medical-Dental Service Bureau, Inc.	$198,703 26	$118,237.37
Central Admitting Bureau for Hospitals	241,943 75	181,584.96
Total	$440,647.01	$299,822.33

Slightly more than 70 per cent of the entire business has been collected and disbursed to the professions involved. The average term of payment arranged for is about 8 months; therefore, a large amount included in the outstanding accounts is not yet due. When it is considered that these accounts are the most hazardous of all types of accounts, it must be admitted that this is a remarkable showing. It must also be borne in mind that the Bureau is passing out of the experimental stage and the quality of work shoul dimprove in the future as a result of past experience.

Attention must be focused on the fact that the Medical-Dental Service Bureau is performing a social function and aiding in providing health security for the community by coöperating with the Central Admitting Bureau for Hospitals. The Central Admitting Bureau for Hospitals has referred many of its applicants who were not entitled to help from community funds to the Medical-Dental Service Bureau. On the other hand the Medical-Dental Service Bureau has directed many deserving persons who were unable to pay as private patients to the Central Admitting Bureau for Hospitals. These two Bureaus in coöperation with the Board of Public Welfare are equipped to supply the medical needs of all who apply, in accordance with their economic status.

Approximately 25 per cent of all persons who apply are referred to the Bureau by friends or employers. This fact demonstrates the popularity of the Bureau and insures the permanency of its existence.

The accomplishments of the Bureau can, in a small measure, be summarized by the following:

1. The public is slowly being educated to the fact that health bills are just as important as any type and must be paid in order to maintain a credit standing. (The Bureau is affiliated with the National Retail Credit Association.)

2. Many persons have received medical and dental care from private doctors who would otherwise have applied to clinics and charity institutions.

3. Many persons are diverted to charity and community funds who cannot afford to pay medical and dental bills. (A thorough investigation is made of each case.)

4. A complete socio-economic picture is given for each patient, and the doctor or hospital knows exactly what procedure is best to follow in each case.

5. Through this picture the doctor is able to determine whether or not his fee is commensurate with the patient's ability to pay, and many fees are adjusted accordingly.

6. Persons are being educated to prepare for obstetrical cases and for elective treatment by paying in advance on both the doctor's and hospital's bills through the Bureau. (This is not prepayment as generally meant, since the patient is preparing to pay a known, definite obligation.)

7. The Bureau has, approximately, 10,000 complete records, including those from the Central Admitting Bureau for Hospitals. These records are of those persons who have made arrangements to pay their bills through the Medical-Dental Service Bureau. They are accessible to any doctor or hospital for reference purposes regarding paying habits. The use of these records will be extremely

helpful to doctors or hospitals wishing to extend credit.

8. The Bureau has progressed and at the same time maintained the ideals upon which it was established; hence, it is now recognized as an integral part of the outstanding "Health Security for All" program in the United States.

The year of 1936 marked the installation of machine bookkeeping in the Medical-Dental Service Bureau. This became a necessity because of the volume of work and inaccuracy connected with hand posting. Although the changing of system involved a great amount of expense and labor the results are now quite apparent. All employees worked long hours. Some worked a few nights without any rest whatsoever, and, without exception, each employee toiled through the summer months without any vacation in order to make this change of system possible. The quality of the work has improved, and much time, formerly consumed by bookkeeping, is directed toward improving collections.

Too much praise cannot be given to those physicians who released their deserving patients who required the assistance of community funds to staff physicians. Many physicians having staff privileges gave their services free of charge. Sacrifices of this nature cannot be measured in terms of money nor in amounts of business, but they are necessary to the success of the Medical-Dental Service Bureau.

A perusal of the statement of assets and liabilities, which is included as part of this report, indicates that the Bureau is making a small profit each months. It was found necessary to decrease the overhead, and, in a sense, limit the expansion of the Bureau, due to an existing deficit of $3,000.00 as at September 1, 1936. Since this date the Bureau has been able to make a profit of about $200.00 per month. The deficit is now, approximately, $1,200.00 and the Executive Director feels that this can be entirely wiped out before the summer is over. It is the purpose of the Executive Director to start to liquidate the balance of the loans due the Medical and Dental Societies, before summer has passed, on a definite re-payment basis.

The Executive Director earnestly solicits the continued coöperation of the hospitals and members of the Medical and Dental professions and promises that efforts will be constantly exerted toward improving the quality of work during the coming year.

MEDICAL-DENTAL SERVICE BUREAU, INC.

Harry Trainor, *Executive Director.*

BALANCE SHEET

MEDICAL-DENTAL SERVICE BUREAU, INC.

Washington, D. C.

As at March 31, 1937

ASSETS

Current		
Cash in Bank	$9,989 56	
Petty Cash	50.00	
Cashier Change Fund	25 00	$10,064 56
Trust Accounts Receivable		
Medical-Dental Service Bureau, Inc.	$80,465.89	
Central Admitting Bureau for Hospitals, Inc.	47,668.70	
Trust Accounts Receivable—1935—Doubtful	12,690 09	140,824.68
Fixed		
Furniture and Equipment	$5,028.40	
Less: Reserve for Depreciation	430.27	4,598.13
Deferred Charges		
Unexpired Insurance	$88 82	
Inventory, Printing, Stationery and Office Supplies	225 00	
Inventory, Advertising and Publicity Supplies	60.00	
Prepaid Rent	111.84	485.66
Other Assets		
Advance		200 00
Total Assets		$156,173 03

LIABILITIES AND NET WORTH

Current		
Accounts Payable—Trade Creditors	$2,615.31	
Accounts Payable—Professions	12,705.24	
Notes Payable—Societies	1,700 00	$17,020.55
Trust Accounts Payable		
Medical-Dental Service Bureau, Inc.	$72,419.04	
Central Admitting Bureau, Inc.	42,886.93	
Trust Accounts—1935—Doubtful	11,421.09	126,727.06
Uncollected Fees		14,061.53
Net Worth		
Net Loss for Period Ended August 31, 1936	$2,997.43—	
Less: Profit 7 Months Ended March 31, 1937	1,282.43	1,715 00—
Unlocated Differences		78 89
Total Liabilities and Net Worth		$156,173 03

MEDICAL-DENTAL SERVICE BUREAU, INC.

Washington, D. C.

STATEMENT OF INCOME AND EXPENSE FOR 6 MONTHS' PERIOD, SPETEMBER 1, 1936, TO MARCH 31, 1937

Earned Income	$10,355 15	
Earned Discounts	.67	
Total Income		$10,355.82

Brought Forward		$10,355.82
Operating Expenses		
Salaries	$5,409.94	
Stationery, Printing and Office Supplies	541.92	
Advertising and Publicity	4.12—	
Telephone and Telegraph	553.07	
Postage	457.58	
Insurance	66.98	
Rent	930.98	
Office Maintenance	394.91	
Unemployment Tax	82.17	
Social Security Tax	14.86	
Professional Services	200.00	
Depreciation on Furniture and Equipment	230.00	
Miscellaneous Expense	195.10	
Total Expenses		9,073.39
Net Profit		$1,282.43

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS*

The regular meeting of the Washington Society of Pathologists was called to order at 1:30 P.M., April 3, 1937, in the Army Medical Museum by the President, Dr. R. M. Choisser. There were 20 members present.

Captain Elbert DeCoursey reported that the Articles of Incorporation were duly recorded in the Office of the Recorder of Deeds, Washington, D. C., on April 2, 1937, and the society is now legally "The Washington Society of Pathologists, Incorporated."

Presentation of Cases

Dr. L. L. Ashburn presented slides from the autopsy of a case (presented before the Society at the January, 1937, meeting) of a white man, aged 45 years, who had complained of diarrhea for 6 months, with nausea, vomiting, and bloody mucoid stools. Proctoscopic examination showed a small ulcerated rectal mass which histologically showed the presence of Entameba histolytica- The patient received emetine hydrochloride and carbar. sone. The gastro-intestinal X-ray studies showed improper filling of the duodenal cap. At autopsy there was a bleeding ulcer of the duodenum and numerous apparently healed ulcers of the sigmoid and rectum. Microscopic examination of the colon showed numerous scars of the mucosa and submucosa, completely interrupting the muscularis mucosae.

In the discussion it was said that amebae have never been shown in the intestines above the ileum, although frequently demonstrated in the skin.

Captain Elbert DeCoursey presented (1) the case of a 7 months'-old baby who was brought into the hospital dead. The mother had seen the infant at the time of the evening feeding and did not notice anything unusual until the following morning, at which time it was completely covered with bed-clothing and was dead. The coroner examined the infant and found no particular changes except cyanosis. Microscopically there were a little congestion and edema of the lungs, slight cloudy swelling of the kidneys and a large thymus. The adrenal glands showed calcification in the medulla extending into the inner zone of the cortex.

Discussion centered around the involutional process of inner cortical degeneration and hemorrhage after birth which might have been unusually stormy in this case resulting in calcification and necrosis, but having nothing to do with the death of the child.

Captain DeCoursey presented (2) intestine, lung, and kidney of a case, which were recently sent in from Panama, of a middle-aged man whose cause of death was unknown. The patient had had syphilis followed by bismuth therapy. He was treated by X-ray for a bismuth dermatitis. There were numerous dark colored, elevated nodules, 1 to 2 cm. in diameter on the mucosa of the large intestine and a few in the lungs, pharynx, kidneys. The intestinal lesions were striking.

In the discussion the similarity of Kaposi's hemorrhagic sarcoma, hemorrhagic lymphosarcoma, and melanomatosis were mentioned.

Captain DeCoursey also presented (3) the gross specimens of 2 hearts showing gonococcic endocarditis of the aortic valve. The blood cultures had been positive for gonococci. Microscopic slides from these valves also showed gram-negative diplococci. These hearts will be described by Captain R. M. Thompson in an article to appear in the Military Surgeon.

Captain DeCoursey presented (4) the case of a 7 months'-old colored baby which was brought in dead from the Panama jungles. At autopsy there were a few areas of consolidation in the lung and an enlarged pale heart which the pathologist interpreted as cloudy swelling secondary to bronchopneumonia. Sections revealed the myocardium filled with a chronic inflammatory cell exudate plus many leishmaniform bodies of the Trypanosoma cruzi, characteristic of Chagas's disease. The thyroid gland was not involved. Also, in the brain there were found flame-shaped inflammatory lesions and occasional nests of leishmaniform T. cruzi. This was the first fatal case reported in Panama.

In the discussion, **Dr. J. W. Miller,** who reported the first clinical cases of Chagas's disease in Panama, told of the recent findings of triatomes in Florida naturally infected with T. cruzi, and that the disease probably was present in the United States.

Lieutenant Colonel J. E. Ash presented an ovarian tumor from a woman, aged 43 years, who complained of severe low pelvic pains. An anterior and posterior colporrhaphy, right oophorectomy and salpingectomy, and ligament suspension were done. There was present a cyst 8 cm. in its greatest diameter, which contained numerous hair follicles. Microscopically, the ovarian tumor is made up of cysts of various sizes. There are masses of sebaceous glands and hair follicles and an island of thyroid gland tissue. No mesenchymal structure is noted, but there are both entodermal and extodermal elements.

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* Transactions of the March meeting were omitted because of length. They may be published during the summer.

Dr. Walter Freeman presented (1) the case of a white woman, aged 27 years, whose onset of illness occurred November 15 with severe frontal headache, stiffness of the neck, dizziness, staggering, nausea, and prostration. Urinary incontinence developed about December 1. Examination showed euphoria, apathy and blunting of intellectual facilities; sense of smell absent on left; marked choked discs; weakness on the right side with a positive Babinski sign. The spinal fluid was under 360 mm. of pressure, otherwise negative. The patient died on December 13. Autopsy revealed a large glioma in the left frontal pole with marked pressure manifestations. The tumor is of interest on account of the variety of cell types in different locations, some resembling fibrillary astrocytoma; others a highly malignant spongioblastoma. The reason for presenting this case is because of the variety of cell types in the tumor, fibrillar astrocytoma, giant cells, a spongioblastoma multiforme. This brings out an interesting point in that it is bordering on a rather benign blastocytoma.

Dr. Freeman also presented (2) the case of a white man, aged 45 years, whose onset of illness began February 20 with some staggering. Sluggishness occurred next day, then confusion, mumbling speech and repetition of phrases. When seen on February 22 he was aphasic and slightly weak in the right hand. There was no fever or other disturbance. A diagnosis of mild cerebral thrombosis was made. The following day the temperature rose to 104°F.; the patient was stuporous, showed complete hemiplegia and early choked discs. The spinal fluid was under high pressure and contained 500 leukocytes per cu. mm. The patient died at 9:30 P.M. Examination of the brain revealed a thick purulent exudate over the left hemisphere with upwards of 50 small abscesses, mostly hemorrhagic, scattered through the hemisphere and cerebellum. At autopsy, 12 hours after death, a culture yielded a small granulated bacillus (Lactobacillus aerogenes). A small primary focus was found in the lung.

In the discussion, the common occurrence of colon bacilli as a contaminant in cadavers was noted.

Dr. Tomas Cajigas presented a tumor of the ovary from a woman, aged 49 years, who had an enlargement of the abdomen only 1 month before consulting a physician, although the mass in the abdomen had reached the size of a full-term pregnancy. She had passed the menopause and had no uterine bleeding. This tumor is a granuloma-cell carcinoma of the ovary, and the point of interest was mainly the unusually numerous microscopic follicle-like bodies throughout the tumor with many follicle cysts about 5 cm. in diameter.

Dr. Oscar B. Hunter presented the case of a woman, aged 45 years, who had a tumor in the fimbriated end of the left fallopian tube. The Aschheim-Zondek test was negative. Microscopically it is strictly a carcinomatoid cystadenoma.

The meeting adjourned at 3:30 P.M.

COMING MEETINGS

The Washington, D. C., Ophthalmological Society will convene in the auditorium of the Medical Society of the District of Columbia's Building, May 31, at 8 P.M. The program:

Symposium on Cataract

1. "Etiology." Clyde A. Clapp, M.D., of Baltimore.
2. "Preoperative Care and Technic." Edmund B. Spaeth, M.D., of Philadelphia.
3. "Postoperative Care and Complications." Conrad Berens, M.D., of New York.
4. "Varieties in Age." Robert Von der Heydt, M.D., of Chicago.
5. "Histopathology." Lieutenant Colonel J. E. Ash, Army Medical Museum.

The American Medical Association, Eighty-eighth Session, Atlantic City, N. J., June 7–11, 1937. The Medical Society of the District of Columbia wants and will have a large delegation. Let us try to have the largest percentage of members present of any state constituent body. Our membership will be well represented in the program. Dr. Henry C. Macatee is our Delegate to the House of Delegates.

Papers will be read by—

E. A. MERRITT and R. RHETT RATHBONE. "The Heavily Filtered Roentgen Treatment of Superficial Epitheliomas," Section on Radiology.

ROBERT E. MORAN. "Surgical Corrections for Enophthalmos and Exophthalmos," Section on Ophthalmology.

CLAUDE MOORE. "A Survey of the Undergraduate Teaching of Radiology in the Medical Schools of the United States," Section on Radiology.

BENJAMIN RONES. "Formation of Drusen of the Lamina Vitrea," Section on Ophthalmology.

NORMAN P. SCALA, jointly with Ernest A. Spiegel, Philadelphia. "Ocular Disturbances in Lesions of the Mesencephalic Central Gray Matter," Section on Ophthalmology.

JAMES W. WATTS and WALTER FREEMAN. "Psychosurgery: Effect on Certain Mental Symptoms of Surgical Interruption of Pathways in the Frontal Lobe," Section on Nervous and Mental Diseases.

WALLACE M. YATER and EUGENE R. WHITMORE. "A Pathologic Study of 75 Patients Injected with Thorium Dioxide Sol for the Purpose of Making Hepatosplenograms," Section on Radiology.

Participants in formal discussion of papers include—

H. H. Donnally, discussion of paper, entitled, "Isolation Technic: Its History and Results," by Philip M. Stimson, New York City, before the Section on Pediatrics.

Henry B. Gwynn, discussion of papers in a symposium on "Gococcic Infections," before the Section on Urology.

R. M. LeComte, discussion of paper, entitled, "Undergraduate Urologic Instruction," by Roger W. Barnes, Los Angeles, before the Section on Urology.

James W. Watts, discussion of paper, entitled, "A New Test for Diagnosis of Certain Headaches: The Cephalalgiogram," by Temple S. Fay, Philadelphia, before the Section on Nervous and Mental Diseases.

Wallace M. Yater, discussion of paper, entitled, "The Treatment of Coronary Sclerosis of Producing a New Blood Supply to the Heart," by Harold Feil and Claude S. Beck, Cleveland, before the Section on Pharmacology and Therapeutics.

Scientific Exhibits will be participated in by—

Claude Moore. The Teaching of Radiology in the Medical Schools.

Norman P. Scala, jointly with E. A. Spiegel and Mona Spiegel-Adolf, Philadelphia, and J. B. Price, Norristown, Pa. Physiopathology of the Sixth Sense.

W. Calhoun Stirling and A. M. Lands. An Experimental and Clinical Study of Traumatic Kidney Injuries.

J. Russell Verbrycke, Jr. Gallbladder Facts and Aphorisms.

Charles S. White and J. Lloyd Collins, George Washington University School of Medicine. Empyema Thoracis.

Eugene R. Whitmore, Georgetown University School of Medicine. Whole Organ Sections, Gross and Microscopic.

The Academy of Medicine of Washington, D. C., was the guest of the Medical Society of the District of Columbia on the evening of May 18, on which date in the Society's auditorium the Academy held an open meeting addressed by Sir Henry Dale, whose subject was "Chemical Transmission of the Nerve Impulse."

What happens at synapses and at the nerve endings in muscle is a question of fundamental interest in medicine. Dr. Dale is a pioneer in discoveries in this field.

The American Heart Association's Fourteenth Annual Scientific Meeting will be held in the Viking Room, Hotel Haddon Hall, Atlantic City, N. J. A program by the Section for the Study of the Peripheral Circulation will be given on Monday, June 7, with a dinner meeting for the Fellows of that Section on the same evening. The general program follows on Tuesday, June 8; a dinner meeting, open to all members and friends of the Association, will be held that evening. Among the papers to be presented are noted the following:

Auricular Fibrillation Treated by Quinidine Intravenously; Acute Arterial Occlusion; Familial Heart Disease; Respiratory Changes in the Cardiac Patient by Rebreathing Experimentation; The Precipitating Causes of Congestive Heart Failure; Clinical Study of a Preparation of Squibb (Urginin) in the Treatment of Myocardial Insufficiency; Heart Disease and Pregnancy; The Diagnosis and Treatment of Chronic Constrictive Pericarditis; The Production of Heart Murmurs by Friction of Serous Surfaces; Effect of Digitalis on Limitation of Cardiac Hypertrophy; Causation and Clinical Diagnosis of Pulmonary Insufficiency (Proven Cases); Acute and Chronic Compression of the Heart; Mechanism of Certain Types of Hypertension. Inclusive will be a paper by **Dr. Wallace Mason Yater**, entitled, "The Histopathologic Basis of Bundle-branch Block."

Wilbur Henry Reitz Brandenburg
(1877–1937)

Dr. W. H. R. Brandenburg, who was graduated from the Columbian (now George Washington) University, 1903, and who was active in the general practice of his profession in Washington, D. C., following internship at Bellevue Hospital, New York City, and Garfield Memorial Hospital, died on May 11, 1937. His membership in the Medical Society of the District of Columbia dates from October 4, 1904, his seniority number being 360. He became a member of the Board of Police and Fire Surgeons of the District of Columbia on October 18, 1907, which position he held at the time of his death. He was the oldest member of the Board in point of service. He held membership in the Columbia Country Club and in the Masonic Fraternity. Dr. Brandenburg was the son of the late Frederick H. and Gertrude E. Brandenburg. A brother was the late Edwin C. Brandenburg, who for years was a prominent local lawyer. He is survived by a brother, Clarence A. Brandenburg, Denver, Colorado. Funeral services were held in the Oak Hill Cemetery Chapel on the afternoon of May 13. The Reverend J. Harvey Dunham, pastor of Western Presbyterian Church, officiated.

MEDICAL ANNALS
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THE USE OF PROTAMINE INSULIN IN THE TREATMENT OF DIABETES MELLITUS*

JANVIER W. LINDSAY, M.D., E. CLARENCE RICE, M.D., MAURICE A. SELINGER, M.D., AND K. HAMMOND MISH, M.D.
Washington

Since the beginning of the use of insulin in the treatment of diabetes mellitus it would appear that no other chronic disease is subject to more exact or better control than has been possible through the proper administration of this preparation in connection with a measured diet. With the improvement in the methods of purification of insulin there has been noted a corresponding increase in the speed of its action, and correspondingly the duration of its effect has become less prolonged. Due to these factors there is often observed a marked and rapid fluctuation in the blood sugar between high and low levels, frequently with the disagreeable train of symptoms attending sudden hypoglycemia. Along with the somewhat limited span of its effective action it not infrequently becomes necessary to inject insulin as often as 2 to 5 times daily, the time of administration sometimes occurring at hours during the day or night which may not only be inconvenient to the patient but may interfere with normal physiological processes, such as obtaining the proper amount of uninterrupted sleep.

While the number of injections of insulin and the time of administration may not be of prime importance to the physician, one must recognize that they have a definite bearing on the morale of the patient. The real problem is the control of the disease.

For the severe diabetic several injections of regular insulin must be given during each 24-hour period. Many attempts have been made to obtain a more even distribution of the effects of insulin by administering it in oil, etc., but no notable success was observed until Hagedorn and his associates prepared a relatively insoluble compound by mixing the sperm of the rainbow trout (*Salmo iridius*) with insulin in a properly buffered solution. This was called protamine insulinate.

The duration of effective action of protamine insulinate, more commonly known as protamine insulin, was found to be from 12 to 16 hours, in contrast to a span of from 6 to 8 hours for regular insulin. By adding zinc to protamine insulin, as suggested by Scott and Fisher, it has been possible to further increase the effective range of action to 20 or even 30 hours.

With this latter compound it now seems possible in the treatment of most patients requiring more than 10 units of regular insulin, given in 2 to 5 injections daily, to substitute 1 dose of protamine zinc insulin with an occasional injection of regular insulin and to achieve better control of the diabetic condition. Joslin has been so impressed with the effectiveness of protamine and insulin compounds, that he has designated that period of diabetic therapy since its use as the Hagedorn Era in contrast with the Banting Era preceding it. During a recent address given at the United States Naval Medical School he stated that if a patient's diabetes was not controlled for as short a time as 6 hours during each 24-hour period, in the course of 10 years this would represent approximately 2½ years during which the disease was not adequately treated. He believes that the proper use of protamine zinc insulin will make it possible to control the carbohydrate metabolism of most severe diabetics during the entire day. We do not believe that the postprandial rise in blood sugar noted by Sindoni in patients taking protamine insulin would be observed frequently if the division of carbohydrate into 6 feedings, as recommended by Joslin and described later in this article, were followed.

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* From the Garfield Memorial and Children's Hospitals.

Experience With Sixty-five Patients

Our experience with combinations of protamine and insulin dates back to January, 1936, since which time a total of 65 patients have been under treatment at one time or another. At first the results were not as satisfactory as we had anticipated. Early in our work with these mixtures we found that there was a great individual variation in reaction to such preparations. Some patients required from 5 to 10 days to effect a satisfactory transfer from regular insulin to the protamine compound, and for 1 patient an adjustment period of 6 weeks elapsed before satisfactory control was obtained. Part of this difficulty was due to the fact that only those patients with the more severe types of diabetes mellitus were given protamine insulin. Most of these were taking from 30 to 70 units of regular insulin a day, 3 to 5 injections being required each 24 hours. During this early period of our use of protamine insulin the maximum dose did not exceed 40 units, and when larger doses were required the compound was given in 2 doses, the larger in the morning before breakfast. Later we have given as much as 90 units of protamine zinc insulin at 1 dose.

With the use of protamine insulin to which small amounts of zinc were added, there was noted a definite improvement in the effectiveness of this preparation. More constant results also have been obtained since the protamine buffer solution and insulin were mixed by the manufacturer instead of by the patient as originally required.

This discussion is based upon the treatment of 65 patients with protamine insulin,* of whom 48 were adults and 17 children. The youngest patient treated was 4 years of age, and the oldest 75 years.

In the beginning the use of the preparation was limited to those patients who were taking from 2 to 5 doses of regular insulin daily and who were classified as severe or moderately severe in type. Later we included those diabetics with vascular complications. Afterwards children were tried on the new preparation.

Our method of transferring the adult patient from regular insulin to the new compound, or for the initial use of protamine insulin in a person who has never received insulin previously, is essentially the same. In either case hospitalization of the patient is desirable. The initial diet for an adult usually consists of from 110 to 140 grams of carbohydrate, 50 grams of protein and 70 to 80 grams of fat. Six feedings are given, breakfast and dinner being 11 to 12 hours apart, lunch midway between. Between meals and bedtime feedings are also given. Carbohydrate is usually divided as follows: 2/12, 1/12, 3/12, 1/12, 3/12, 2/12. By using such a division of carbohydrate, reactions are reduced in frequency and severity.

The dosage of unmodified insulin may first be established by the usual "trial and error" method, based on blood-sugar estimations made fasting and 2 to 3 hours after meals, along with qualitative urinalyses done just before meals, and 12-hour quantitative specimens. If, for example, the average daily requirement was found to be 30 units, a smaller number of units of the new compound, for instance, 20 units, would be given at 7 A.M. on the day the change was contemplated. In addition, 10 units of unmodified insulin would be given just before breakfast. On the following morning the protamine insulin would be increased to about 26 units, and regular insulin given before breakfast depending upon the degree of glycosuria, in the following dosage,

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* Since August, 1936, protamine zinc insulin has been used. The preparations have been supplied by Eli Lilly & Company, Indianapolis, Indiana.

B°	G+	Y++	O+++	R+++.*
0	0	4	6	8

From this point on an attempt would be made to control the patient on protamine insulin alone, from 48 to 96 hours being required to effect the change. When a satisfactory adjustment of dosage has been made it is usually possible and desirable to reduce the dosage after a few days to prevent reactions.

In some patients it has been necessary to continue the use of both preparations. In such cases, the unmodified has been injected just before breakfast and the mixture on arising in the morning.

The use of 12-hour quantitative estimations of urinary sugar in addition to the usual qualitative analyses done before meals has been of considerable value in the control of the patient who is using protamine zinc insulin. In this manner we are able to determine at what period of the day the greatest loss of sugar is occurring, to estimate the optimum time for the administration of the new compound, to determine the necessity for using supplemental doses of regular insulin and to make readjustments of the diet when necessary.

As in the case of regular insulin, we believe that frequent blood-sugar estimations made at intervals during the day are of more value in the control of these patients than the single fasting blood sugar so often advocated. It has been our practice in uncomplicated cases to obtain specimens at 7 A.M., 11 A.M., 5 P.M., and 10 P.M. These, in conjunction with the 12-hour quantitative estimations of urinary sugar, have enabled us to know at approximately what time of day the greatest peak in blood sugar may be expected and to give insulin accordingly.

Results With New Preparation

Of the 62 patients thus treated, 51 were considered to have been satisfactorily controlled, while 11 were not. Age had no effect upon the result.

These patients have been further subdivided into groups whose condition was considered improved, those whose condition remained the same, and those who were definitely worse. These latter 3 groups were then each divided into private patients, ward and clinic patients. Of the 42 private patients treated, 30 improved, 8 remained the same, and 4 became worse. Of 20 ward and clinic patients, 12 improved, 1 remained the same, and 7 became worse. The percentage of failures in the private patient group was 9.52 per cent, while in the ward and clinic group it was 35 per cent.

In Table I, we have presented a summary of the results obtained with protamine insulin in regard to diet, the number of injections required per day and the presence or absence of reactions. Whenever the patient had previously taken regular insulin, a comparison of results is offered.

From this table it is seen that of the 52 patients who had received unmodified insulin prior to the administration of protamine insulin, it was possible to reduce the number of injections required daily in 38 cases. In 11, no changes were made, while in only 3 instances was it necessary to increase the number of injections.

It will be noted that in 18 patients we were able to increase the diet while they were under treatment with the new compound. In 3 others a reduction in the diet was required, while in the remaining 31 cases the quantity of food allowed was kept the same as it had been while regular insulin was being used.

Insulin Reactions

The manifestations of insulin reaction with this new preparation were in general similar to those experienced with the ordinary form of

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* B° means blue or no sugar; G+ means green or small amount of sugar; Y++ means yellow or fairly large amount of sugar; O+++ and R+++ mean orange and red or large amount of sugar.

TABLE I

Results of Treatment With Protamine Insulin

CASE NUMBER	AGE YEARS	COLOR	NUMBER OF INJECTIONS REQUIRED DAILY REGULAR INSULIN (AVERAGE)	REACTIONS 1+ SLIGHT 2+ MOD. SEVERE 3+ SEMICOMA 4+ COMATOSE	DIET	NUMBER OF INJECTIONS REQUIRED DAILY PROTAMINE } INSULIN REGULAR (AVERAGE)	REACTIONS 1+ SLIGHT 2+ MOD. SEVERE 3+ SEMICOMA 4+ COMATOSE	RESULTS
1	7	W				1	Some 2+	Improved
2	7	W	2	Many 3+	Increased	1.5	Some 2+	Improved
3	8	C	2.5	Occ. 1+	Increased	2	Several 3+	Improved
4	10	W	3	Occ. 4+	Increased	1.5	Few 3+	Improved
5	10	W	3	0	Increased	2	0	Improved
6	11	W	3.5	Several 4+	Same	2	Several 2+	Same
7	11	W	2	0	Same	1	0	Improved
8	12	W	1	1+	Increased	1.2	Several 2+	Improved
9	14	W	2	Several 2+	Increased	2	Several 2+	Improved
10	15	W	4	2+	Increased	3	0	Worse
11	16	W	3	0	Same	2	0	Improved
12	17	W				1	0	Improved
13	18	W	5	0	Decreased	3	0	Worse
14	19	W	4	Some 2+	Same	2	Several 2+	Improved
15	20	W	3	0	Increased	1	0	Same
16	36	W	2	Occ. 2+	Same	2	0	Same
17	61	W	1	0	Same	1	0	Improved
18	34	W	2	Occ. 2+	Increased	2	Occ. 3+	Improved
19	57	W	4	Occ. 2+	Increased	1	0	Improved
20	67	W	3	Several 3+	Same	3	Occ. 1+	Improved
21	61	W	2.5	Several 1+	Same	1.5	Occ. 2+	Same
22	55	W	2	Occ. 2+	Same	2	0	Same
23	42	W	2	Several 2+	Same	1	Occ. 1+	Improved
24	67	W	3	0	Same	1	?	Improved
25	49	W	3	Some 4+	Increased	2	Some 4+	Worse
26	46	W	3	Some 3+	Same	3	Some 3+	Same
27	53	W	3	Some 3+	Same	3	Some 3+	Same
28	31	W	3	Some 2+	Same	2	0	Improved
29	54	W	1	0	Decreased	1	0	Improved
30	60	W				1	0	Improved
31	22	W	4	Many 2+	Same	2	0	Improved
32	53	C	3	Some 1+	Increased	1	0	Improved
33	72	C	3	0	Same	1	0	Improved
34	53	W	2	0	Increased	1	0	Improved
35	45	W	3	Occ. 1+	Increased	1	0	Improved
36	40	C	3	0	Same	1	0	Improved
37	68	W	4	0	Increased	1	0	Improved
38	73	W				1	0	Improved
39	50	W	2	Many 2+	Same	1	Several 4+	Worse
40	32	W	2	Occ. 2+	Same	1	0	Improved
41	47	C	4	?	Same	1	?	?
42	52	C	3	0	Same	1	0	Improved
43	40	W				1	0	Improved
44	40	W	2	1+	?	1	0	?
45	63	W	1	?	Reduced	2	0	Same
46	75	W	1.5	0	Increased	1	0	Improved
47	52	W	2	0	Same	1	0	Same
48	29	W				1	0	Improved
49	24	W					2	Improved
50	50	C	2	0	Same	1	0	Worse

TABLE I—*Concluded*

CASE NUMBER	AGE YEARS	COLOR	NUMBER OF INJECTIONS REQUIRED DAILY REGULAR INSULIN (AVERAGE)	REACTIONS 1+ SLIGHT 2+ MOD. SEVERE 3+ SEMICOMA 4+ COMATOSE	DIET	NUMBER OF INJECTIONS REQUIRED DAILY PROTAMINE REGULAR INSULIN (AVERAGE)	REACTIONS 1+ SLIGHT 2+ MOD. SEVERE 3+ SEMICOMA 4+ COMATOSE	RESULTS
51	45	C	3	0	Same	2	0	Worse
52	48	C	1.5	0	Same	2	0	Worse
53	44	W	3	0	Same	2	Occ. 1+	Worse
54	47	C	1	0	Same	1	0	Improved
55	21	W	1	Some 3+	Same	1	Some 3+	Same
56	55	W	2.5	Occ. 1+	Same	2	0	Improved
57	49	W	3	Rare 4+ Some 2+	Same	2	Many 2+ Occ. 3+ Occ. 4+	Died
58	39	C	3	0	Increased	1	0	Improved
59	4	W	1	One 4 +	Same	1	Occ. 3+	Worse
60	65	W				2	0	Improved

insulin. They consisted of nausea, headache, fatigue, drowsiness, weakness, nervousness, sweating, tingling sensations in the extremities, unconsciousness and convulsions. They were relieved by the administration of carbohydrate, but it was often necessary to continue this at intervals of several hours, due to the slow absorption of protamine insulin causing secondary reactions. Owing to the slowness with which it lowers the blood sugar level, protamine insulin may occasionally produce marked hypoglycemia without apparent symptoms. This was notable in the case of one of our juvenile patients. This child on several occasions was found to have a blood sugar in the morning of 0 mg. per 100 cc. of blood, yet at these times he did not present any of the symptoms of insulin shock.

In another case the hypoglycemia produced by the new compound was believed to have been a contributory factor in the death of the patient in whom there was marked cerebral arteriosclerosis. This case is being reported elsewhere in detail (Lindsay, Rice, Selinger and Mish).

Of the patients treated in this series 40 had no reactions, while 20 complained of reactions on one or more occasions. Of these latter cases, 2 suffered only an occasional slight reaction. In 8 there were several moderately severe reactions. In 7 patients a condition of semicoma was produced one or more times, and in 3 instances a comatose condition resulted.

The time of day at which these reactions occurred is of importance. This is illustrated in Table II.

TABLE II

TIME OF REACTIONS

HOUR OF ADMINISTRATION OF PROTAMINE INSULIN	NUMBER OF CASES HAVING REACTIONS	TIME OF REACTIONS
6 A.M.	2	5 A.M. to 10 A.M. (1)* 9 P.M. to 10 P.M. (1)
7 A.M.	12	6 A.M. (3) 5 A.M. to 6 A.M. (1) 4 A.M. to 6 A.M. (1) 5 A.M. to 8 A.M. (1) 11 A.M. (1) 6 A.M. to 11 A.M. (1) 11 A.M. to 5 P.M. (1) 1 A.M. to 2 A.M., and 5 A.M. to 6 A.M. (1) 1 A.M., and 11 A.M. to 3 P.M. (1) 4 P.M. to 5 P.M. (1)
8 A.M.	1	4 A.M. to 5 A.M.
12 Noon	1	4 A.M. to 5 A.M.
5 P.M.	2	1 A.M. to 2 A.M. (1) 11 A.M. (1)
7:30 P.M.	1	8 A.M. to 12 Noon
6 A.M. and 6 P.M.	1	Some reactions in morning; others at night; few lasted all day

* Figures in parentheses refer to number of cases.

TIME OF ADMINISTRATION

In the majority of patients, the preparation was taken at 7 o'clock in the morning, 43 of our cases receiving it at this hour. In 6 of the remaining 18 patients, the compound was injected at various hours of the morning ranging from 6:30 A.M. to noon. Another group of 6 received it in the evening from 5 P.M. to 7:30 P.M. The remainder required 2 doses daily, 1 in the morning and another in the evening, approximately 12 hours apart.

When it was necessary to use both drugs, the regular insulin usually was given once daily before breakfast, occasionally in the middle of the day, and very rarely a few units just before the evening meal.

In general, it may be stated that 1 injection of protamine zinc insulin given on rising in the morning will ordinarily be sufficient provided its effect is maintained for a period of approximately 30 hours. When this is manifested for a shorter period of from 18 to 22 hours, supplemental doses of regular insulin are given just before eating breakfast. These general statements will not apply to all patients, indeed each must be individualized. If reactions occur regularly and are severe during the late evening or early morning in spite of adjustment of the intake of carbohydrate, it will be necessary to move the time for the administration of protamine insulin to a later hour. The use of an amount of the modified insulin insufficient to produce a 28- to 30-hour effect will require an additional injection of unmodified insulin with resultant flexibility of dosage which may be of distinct advantage from the standpoint of the elimination of reactions and maintenance of a more normal blood sugar level. This method has been of particular advantage in the treatment of young patients and may be found of value in the better control of members of the older group.

We have used as a criterion of satisfactory results the following conditions: (1) The maintenance of the blood-sugar concentration at or near the normal level during the 24 hours, (2) the absence of, or fewer and less severe, reactions than with regular insulin, (3) a reduction in the number of doses of insulin in 24 hours, (4) a feeling of well-being and improvement in the patient's general condition.

An attempt has been made to analyze the 11 cases in which protamine insulin treatment has failed with a view to learning the cause for this. Upon reviewing the records of these patients it was found that in 7 the mentality of the patient was not sufficient to grasp the intricacies of the protamine insulin therapy in addition to the usual diabetic régime. In another patient there was a lack of coöperation. Of the remaining 3 cases, 1 was complicated by pulmonary tuberculosis and endocrine disturbances incident to the menopause, while the other 2 were patients in whom frequent and severe reactions producing unconsciousness made it necessary to discontinue the new form of insulin.

USE IN SURGERY

In 8 patients we have used protamine insulin to supplement the effect of regular insulin during surgical operations. The types of operations are: Repair of ventral hernia, bilateral inguinal herniotomy, mid-thigh amputation, prostatectomy, amputation of toe, curettage of osteomyelitis of heel, ruptured ectopic pregnancy, incision and drainage of abscess of chest wall, and excision of carbuncle.

No attempt has been made to substitute the old insulin entirely by the new compound. Due to its rapid action the greatest dependence is placed on the former. Instead, it has been administered with the idea of preventing the wide fluctuations in blood sugar so common after an operation. It has been our practice to continue the usual postoperative regimen of frequent feedings of liquid carbohydrate by mouth or dextrose intravenously or subcutaneously as indicated, along with regular insulin as required by the degree of glycosuria and glycemia present. In addition protamine insulin has usually been given in 2 doses at 12-hour intervals, in an attempt to give the patient a longer period of rest at night without the need of disturbing him one or more times for feedings and regular insulin.

In this manner it has often been possible to allow the patient to obtain uninterrupted rest from 10 P.M. to 6 A.M., even in the presence of an acute infection.

In the preoperative administration of this new compound, we have attempted to give it at such a time that its action would coincide with the expected rise in blood sugar due to the anesthetic.

Use in Infections, Vomiting and Diarrhea

Protamine insulin has been used in patients having infections such as colds, sore throats, influenza and measles. Our method has been to continue to have the patient inject it at the same time he had been receiving it prior to the onset of the infection. However, the number of units has usually been increased somewhat. If the first urinalysis in the morning consistently showed sugar, the dose is gradually raised, and if necessary regular insulin is given every 4 hours during the day along with a feeding, the dosage depending upon the degree of glycosuria, proportionally smaller amounts being given during the latter part of the day. Here again, it has usually been possible to allow the patient to go from 8 to 10 hours at night without urinalyses or insulin, with no danger from acidosis.

In cases of vomiting and diarrhea, we have considered it best to discontinue the use of protamine insulin for the time being, and return the patient to the use of regular insulin at 4-hour intervals along with feedings of liquid carbohydrate as indicated by examination of the blood and urine.

Use in Malnutrition

In addition to the 65 cases of diabetes treated with this new preparation, it was used in 4 additional cases of malnutrition in which there was no evidence of organic disease as a cause of the under-nutrition. In general, the results obtained with this compound were not as satisfactory as with the unmodified form of insulin. Two of the patients reported no improvement in appetite. The other 2 patients stated that there was an increased desire for food, but not as great as with regular insulin. It is interesting to note that with one of the latter patients who was benefited by protamine insulin and received it at intervals of 48 hours the stimulation to appetite continued through the second day.

Skin Reactions and Allergy

A few patients have mentioned that protamine insulin has caused irritation of the skin, especially when large doses were used, but on further use they either became accustomed to this effect or it evidently subsided.

Indications and Contraindications

We have attempted to classify the type of diabetic patient in whom we believe protamine insulin to be indicated. Those who are well controlled on from 1 to 2 doses of regular insulin need not be placed on the newer drug. Those of limited intelligence are not fit subjects for protamine insulin therapy, since they cannot comprehend the more intricate details of this type of treatment. Its use should be denied those patients who cannot be kept under rather constant supervision.

It is, however, of considerable value in the treatment of children, due to the fact that it does away with sudden and violent fluctuations in blood sugar. While the blood sugar may be low, it does not usually cause the severe reactions as are sometimes noted during the use of regular insulin.

In cardiac cases it likewise seems indicated for the reason that it does not subject the patient to the sudden fall of blood sugar which is so undesirable. It is known that in diabetes the glycogen in cardiac muscle is high in contradistinction to the glycogen in the other muscles of the body where it is low. This is supposedly to protect the heart and make it as easy as possible for the available insulin in the body to act. Hence the use of the slow-acting protamine insulin will serve to protect this mechanism.

Summary

1. Sixty-five diabetic patients were treated with protamine insulin. Of this number, 51 were satisfactorily controlled, while 11 were not. Of these latter, 7 were ward and clinic patients

and 4 private patients. Three cases could not be classified; 2 left the hospital at their own request during the course of an active infection, and the third, a very elderly patient, was admitted to the ward with death imminent due to the toxic effect produced by diabetic gangrene.

2. Protamine insulin has a definite use in surgery inasmuch as it allows the patient longer periods of rest at night without the need of interrupting him one or more times for feedings and regular insulin and tends to prevent the extreme fluctuations in the blood-sugar level.

3. Reactions were manifested in 20 of these patients on one or more occasions since beginning the use of the new compound. However, since these have been under treatment over a longer period of time, we have been able in many to eliminate these reactions entirely by the readjustment of the diet and by the better timing of the injection of protamine insulin.

4. While protamine insulin represents a distinct therapeutic advance in diabetic control, its use is not applicable to all types of patients, particularly those of inferior mentality. Its use should be denied those who will not coöperate in maintaining contact with the physician.

N.B.: Through the courtesy of Dr. Lewis C. Ecker, diabetic patients on his medical service at the Garfield Memorial Hospital were made available for this study.

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Multiple Sclerosis: Treatment With Quinine Hydrochloride.—It has been definitely recognized for years by all neurologists that the resources in the treatment of encephalo-myelitis disseminata are very limited. Therefore, any suggested treatment, while not accepted as conclusive, if it has a certain amount of scientific justification, is worthy of a trial.

Several years ago, Dr. R. M. Brickner of New York suggested the use of quinine hydrochloride in the treatment of multiple sclerosis. Up to the present time the results have given sufficient promise of benefit to warrant reports of cases receiving this therapy. Brickner recently reviewed his series of cases over a 5-year period and concluded that the statement seems justified that the use of quinine hydrochloride is really beneficial . . .

Case Report.—An American housewife, married, 27 years old, first entered the Guthrie Clinic on October 30, 1934, with a chief complaint of numbness and tingling in the hands and difficulty in walking. . . .

She could ascend stairs and walk on the level as usual but in descent she felt as though her limbs might not bear her weight but she never fell. Throughout September the uncertainty in descent became more marked and by October 1, she had definite difficulty in walking along the street unless she supported herself by holding to the arm of a companion. She did not look at her feet when she walked and the difficulty lay in the feeling of uncertainty that her limbs might not bear her weight. She could walk much better on some days than on others.

The patient had no other symptoms until 3 weeks before admission to the hospital. At that time numbness and tingling in the hands appeared; the numbness was associated with a feeling of cold, while the tingling was associated with a feeling of considerable heat. Immediately following this the patient noted increasing difficulty in writing and that both hands performed acts in a clumsy manner; she had the feeling that her hands had increased in size and that the ends of her fingers were "covered with water blisters." At this time she noted also that there was a hand sensation under both arches as though a strip of adhesive about 2 inches wide was firmly applied under each instep. . . .

Treatment and Progress.—The medication was given first on November 18, 1934, and was prescribed according to the technic advised by Dr. Brickner. The initial dosage was 5 grains of the quinine hydrochloride 3 times a day. As no symptoms of cinchonism developed, the total daily dosage of 15 grs. was continued. From the time when the patient was first seen until treatment was begun most of the symptoms had become worse, particularly the itching, pain and burning of the hands; sleep had become impossible. By the end of the second week of medication she already had improved. The pain in the hands was less frequent and of shorter duration. She was getting a few hours sleep and was able to be up in a wheel chair for a short time daily. Her appetite was better. At the end of another week this improvement had continued. All neurologic symptoms were subsiding. The pain in the hands occurred but twice daily, she was able to walk alone a little each day and slept well without medication. . . .

Comment.—This case review illustrates what decisive indications of improvement are encountered in the treatment of some patients with multiple sclerosis by the use of quinine hydrochloride. The incidence of spontaneous remissions in the disease is well known and, of course, forms a serious obstacle in the evaluation of any type of treatment. However, with such immediate, continuous and apparent complete relief from all symptoms, one cannot help but conclude that this therapy exerted some specific influence on the supposed lipolytic agent. The factors favoring the good response obtained in this case undoubtedly were the age of the patient, the initial attack of the disorder and the short duration of the symptoms.

Quinine hydrochloride therapy should be tried over a long period, however discouraging the outlook may appear. Anyone employing this form of treatment should have a thorough understanding with the patient about the possible irregular behavior of the symptoms while taking the medication, and the absolute necessity of the fullest coöperation. It is to be emphasized that the dosage must be determined separately for each patient. Cinchonism should be avoided because of its deleterious influence on multiple sclerosis.

As far as is known at the present time, the administration of quinine must be continued indefinitely. The medication is best given orally in the form of quinine hydrochloride because it is the most soluble of the salts. It is recommended that more patients with multiple sclerosis be given the benefit of this form of treatment and that they undergo a long period of observation.

Extract from article by STANLEY D. CONKLIN, M.D., Sayre, Pennsylvania, *Guthrie Clinic Bulletin, April, 1937, p. 171.*

GASTROSCOPY*†

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In a diagnostic clinic, as well as private practice, one is often confronted with problems in gastro-enterology, in which the symptoms cannot be adequately correlated with the physical facts. Realizing this inconclusiveness of available methods, it was my good fortune to have the opportunity of visiting the Gastro-intestinal Clinic of the Johns Hopkins Hospital. There I witnessed a diagnostic method which was being used routinely in the management of their vague gastro-intestinal problems. To my astonishment, Dr. James L. Borland was demonstrating gastroscopically gross pathological lesions in the interior of the stomach which in many instances could not be reconciled with the negative gastric X-ray reports.

Seeking further confirmation of this advance in precision, I was prompted to visit Chicago and study with Dr. Rudolf Schindler. In his Gastroscopic Clinics at the Billings, Michael Reese, and Cook County Hospitals, Schindler, with a personal experience of nearly 4,000 gastroscopies, was conducting 5 to 10 daily observations of this nature. These cases referred for gastroscopy presented the most varied problems. In some the gastric complaints had not been solved with the usual methods of study, while in others an opinion was sought as to the nature of detectable X-ray lesions in the stomach. Gastroscopy in most instances settled the questions involved. After such a course I am convinced that many vague diseases of the stomach can be positively diagnosed.

Simply stated, gastroscopy is the intravital inspection of the gastric mucosa, which in recent years has been made possible chiefly through the contributions of Schindler. It was he who in 1932, after working diligently on this problem for years, found his efforts rewarded when he designed and reported the first practical, flexible gastroscope. However, the evolution of this remarkable instrument was based largely on accumulated knowledge handed down years before by other pioneers in this field.

Although gastroscopy is often spoken of as the beginning of a new era in gastro-enterology, its possibilities were recognized as long ago as 1868. At that time Kussmaul devised an open rigid tube, and depended on reflected candle light to illuminate the interior of the stomach. It is singular that his first patient was a sword swallower and one would suppose this would be a distinct advantage. However, his efforts were unsuccessful and were abandoned. Interest was revived again in 1881, when Mikulicz, making use of Edison's newly discovered electric lamp, constructed a rigid tube with an electric lamp at the end and the objective of the optical system proximal to the light. This instrument likewise was abandoned, although some of its principles were fundamentally correct. During the following years many men, notably Nitze, Leiter, and Rosenheim attempted to solve the construction of a practical gastroscope, but were only partially successful.

In 1911, Sussmann introduced the first flexible gastroscope. This instrument was passed into the stomach in a flexible state, and then converted into a rigid tube by means of a locking device. This mechanical straightening was dangerous to the patient, and as a consequence the method was deserted.

Between 1907 and 1921, Jackson, using a rigid open tube, did over 1,700 gastroscopies that are duly recorded. However, many of them were incomplete as compared with the work of the modern flexible gastroscope. Even Schindler, in 1922, constructed a rigid gastroscope which was quite successful in his hands. He was able to examine the interior of the stomach in over 1,300 cases, and in 1923 published a text-book and atlas of gastroscopy on his observations. However, there were a number of objections to this instrument, chiefly that in 40 to 50 per cent of cases it was not possible to introduce the instrument sufficiently deep into the stomach to observe the antrum. The present gastroscope overcomes all these difficulties, and is now used in practically every country in the world. In this connection, I am happy to state that my friend, Dr. John Horan, after training with Schindler, is returning to Melbourne, Australia, to introduce the method in that country.

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* Read before the Section on Internal Medicine of the Society, February 26, 1937.

† From the Clinic of Drs. Clark, King and Geier.

Description of the Schindler Flexible Gastroscope

This ingenious instrument combines safety, visibility, flexibility, and elasticity. The total length, excluding the rubber finger-tip, is 70.5 cm. The proximal half is rigid, being 32 cm. in length and having a diameter of 8.5 mm. The distal half is flexible and elastic, being 38 cm. in length and having a diameter of 11 mm. At the distal end there is a soft rubber finger-tip, an 8-volt electric lamp, objective having a viewing angle of 80°, (50° or 60° may be used), and the complicated optical system containing 46 lenses and covered with 2 thin layers of rubber between which air can be injected into the stomach. The flexible part may be bent to an angle of 34°, without distortion of the circular field of vision. The proximal rigid portion carries the ocular, light switch, and air balloon. The view obtained through the ocular is circular, and the object under inspection is seen with amazing clearness.

The use of air to distend the collapsed stomach walls is desirable for many reasons. In the first place, if water is used for distention, as in cystoscopy, it would be practically impossible to fill the stomach to a sufficient degree without inducing vomiting. Also, water in the stomach quickly becomes turbid from mixture with gastric secretion, and thus obscures good visualization. Air distention results in a greater depth of focus, and in addition the high-lights which run over the surface of the stomach mucosa aid in throwing pathological processes in bold relief. This would not be possible with immersion technic.

To obtain maximum service from the instrument, it should be handled carefully and after each examination cleansed with tincture of green soap and sterilized with alcohol.

Contraindications

In any type of instrumentation, contraindications must be respected. Thus, in gastroscopy a knowledge of the limitations of this important aid to gastro-enterology will serve to advance, rather than halt the progress in this field. Stenosis or obstruction of the esophagus, either organic or spasmodic, is the most important contraindication. This can be ruled out by fluoroscopy, history, or resistance encountered in attempting to pass the Ewald stomach tube. Other contraindications are aneurism, varices of the esophagus, severe kyphoscoliosis, cardiac insufficiency, dyspnea fever, and high blood pressure. In some of the enumerated conditions gastroscopy has been performed, but in the main should be relegated to the more experienced. I recall Schindler's recent patient with angina pectoris, in whom flexible-tube gastroscopy was conducted successfully.

Indications

The indications for gastroscopy are numerous and steadily increasing. This is easily understood when one considers the many cases with vague, undifferentiated gastric complaints, in whom the diagnosis can only be established gastroscopically. Brown has recently stated that any patient of middle age, having unexplained gastro-intestinal symptoms, not responding within a short time to medical management, should have the benefit of gastroscopy.

In addition to being an important aid in differential diagnosis, gastroscopy is advantageous in observing directly all types of chronic gastritis, in following the progress of gastric ulcers, in determining the operability of malignant lesions, in examining postoperative stomachs, in locating the site of bleeding in gastric hemorrhage, in deciding whether a tumor is benign or malignant, and in studying the effect of treatment of the various gastric conditions. These are but a few of the indications for gastroscopy.

TECHNIC OF INSTRUMENTATION

Good descriptions of the technic employed in flexible-tube gastroscopy can be found in the literature. Schindler and later Borland have contributed greatly to this phase of the subject.

The patient must be coöperative and follow all instructions given by the examiner. He should report to the office or clinic on the morning of the examination, having taken no food or water for at least 14 hours.

A hypodermic is given of dilaudid, Gr. $\frac{1}{64}$, or codeine sulphate, Gr. $\frac{1}{2}$, in combination with atropine sulphate, Gr. $\frac{1}{150}$. Forty-five minutes later the oropharynx and oral mucosa are swabbed with 2 per cent pantocain solution. The Schindler special anesthesia tube is then passed, and 5 cc. of 2 per cent pantocain solution containing 5 minims of 1:1,000 adrenalin chloride solution, is forcefully injected into the hypopharynx. This solution emerges as a spray and quickly abolishes the gagging reflex. In 5 minutes this procedure of spraying the hypopharynx is repeated.

An Ewald stomach tube is then passed, the head is placed below the level of the body, and by gravity the stomach is emptied of any retained gastric secretion. The patient then lies on his left side, the left elbow under the body, and his head being supported by the assistant. The instrument is introduced into the stomach as one would pass the stomach tube, avoiding pressure wherever resistance is encountered. It is desirable to reach the lowest depth of the stomach in order to carry out systematic observation of the mucosa. At this point a small amount of air is injected to separate the collapsed stomach wall, and to locate significant landmarks. This can be quite difficult unless one has observed, studied, and appreciated the problems concerned with orientation.

ORIENTATION

The knowledge as to the exact part of the stomach viewed through the gastroscope is difficult, and can only be learned by diligent application of the fundamentals which serve as guides.

Schindler has recorded a very interesting contrast between the interior of the stomach as seen gastroscopically and the gastric anatomy based on anatomical and roentgenological observations. He observed, in over 2,400 gastroscopies, certain structural differences which could not be reconciled with either the X-ray or gross anatomical concepts. The interior of the stomach is separated into two distinct cavities, the body and the antrum, by the musculus sphincter antri. This structure, as seen through the gastroscope, is a prominent fold, having a twisted rope-like appearance, and begins at the end of the parabolic line of the angulus, and runs over the greater curvature and the anterior wall in this region. Its significance from a physiological standpoint is not clearly understood, but Schindler thinks it may prevent food from going too quickly into the antrum. He also believes it is formed by a contraction of circular fibers of the muscularis propria.

Other important observations which he has made are the mobility of the stomach and the inclination of the posterior wall. In the first instance, the stomach has only one fixed point, and that is the cardia; and in the second instance, the posterior wall runs toward the anterior abdominal wall to form an angle with the axis of the esophagus. Gastroscopically then, the nomenclature of the parts of the stomach must be cardia, fornix, anterior and posterior wall, lesser and greater curvature, corpus or body, angulus, musculus sphincter antri, antrum, and pylorus.

The position and shape of the stomach may be altered by many factors, such as the body build, position of the body, and respiratory movements. However, in all cases the gastroscope runs over the posterior wall and lies in close proximity to it throughout the examination.

Schindler has been able to demonstrate graphically these essential points, and in addition has constructed a phantom stomach which exhibits clearly these concepts which are necessary to understand orientation.

Distortions of the gastroscopic picture, at various depths of introduction of the instrument, correspond to the distance between the mucosa and objective.

INTERPRETATION

An understanding of the normal stomach, as seen gastroscopically, is essential in order to evaluate pathological lesions. The color depends a great deal on the color sense of each examiner, but the consensus of opinion is that the normal mucosa is orange-red, with possibly a tinge of yellow present. The folds show up clear and brilliant, being heaviest on the posterior wall, and delicate on the anterior wall. Along the lesser curvature or "magenstrasse" (Aschoff) the mucosa appears smooth, and the antrum also is devoid of folds. It is now generally accepted that the X-ray folds, even with the finest compression technic, do not correspond to the folds as seen through the gastroscope.

Peristalsis can be clearly observed, but usually is limited to the antrum, and begins distally to the musculus sphincter antri. It is a circular movement toward the pylorus, where, upon arrival, a round open hole of the pylorus comes close to form a stellate picture.

The mucous lake is usually seen in the dependent part corresponding to the upper part of the body of the stomach.

Spasms are rarely seen with a flexible gastroscope, whereas with the former rigid instruments multiple spasms were frequently encountered. The X-ray spasmodic hour-glass is practically never seen gastroscopically.

The value of gastroscopy in the recognition of pathological processes in the stomach is now universally accepted. Among other things it has proven conclusively the existence of chronic gastritis, a disease which for many years has been considered doubtful. A search through the literature reveals interesting and pertinent historical facts. The observations and experiments of Beaumont on his patient, Alexis St. Martin, whom Osler called "that old fistulous Alexis," represents a medical contribution of enduring value. During the experiments, and at times in the intervals, St. Martin frequently imbibed too freely of alcohol, or "stimulating" condiments, and Beaumont reported "the diseased appearance of the stomach at this examination was probably the effect of intoxication the day before." Beaumont also observed and described red patches, nodules, aphthous crusts, and pustules. With the exception of the pustules, these conditions have been observed gastroscopically by Schindler, Henning and others. The pustules have never been observed, and no doubt Beaumont in reality was describing either ulcers or erosions.

GASTRITIS

After Beaumont's classical work, gastritis seemed to disappear from the medical literature for many years, although papers by Faber and Einhorn attempted to popularize it. In recent years successful attempts have been made to reconcile microscopic and macroscopic observations in chronic gastritis, by such men as Faber, Stoerk, Konjetzny, and Moutier. With these findings based on his gastroscopic observations, Schindler has proposed a subdivision of chronic gastritis into 3 forms: superficial, atrophic, and hypertrophic. He has since added "gastritis following operation on the stomach." The following is a brief description of these types, as observed gastroscopically.

Superficial Gastritis. Characteristic signs are a patchy redness of the mucosa and edema which is distinguished by a moist, swollen appearance. In addition there is a pathological exudate of thick adherent mucous which varies greatly in color. Occasionally small erosions are seen and the mucosa is inclined to bleed easily. These changes are more marked in the body of the stomach.

Atrophic Gastritis. The mucous membrane has patches of a grayish green color and is thinned out. Heavy, prominent, branching blood vessels are seen in the submucosa. Occasionally true polyps are present. Schindler has demonstrated atrophic gastritis in both young and middle-aged people as well as in the aged. The most striking feature of this disease is the regeneration of the mucosa which has been observed in a number of cases. Jones, Benedict, and Hampton, have observed numerous cases of pernicious anemia with atrophic gastritis, in whom the mucosa regenerated after adequate liver therapy. The relationship between carcinoma and atrophic gastritis is now generally accepted, and it is important to remember in cases of atrophic gastritis that these patients should have the benefit of gastroscopy and X-ray twice a year.

Hypertrophic Gastritis. The mucous membrane has a rather characteristic appearance. It is velvety, plush-like, the high-lights are diminished or absent, and it appears spongy. The folds become enlarged and traversed by creases, giving it a cobblestone appearance. At times these folds are nodular and frequently are the site of small or large hemorrhages. In the antrum one may occasionally observe multiple ulcerations or erosions, having a grayish yellow base. These patients frequently complain of severe ulcer-like pains in the epigastrium, great weakness, and occasionally have a gross hemorrhage from the stomach.

Gastritis Following Operation in the Stomach. Since the advent of gastric surgery, pathological lesions resulting from these operations are frequent. As a result, many patients continue to have symptoms referable to the stomach and are frequently diagnosed psychoneurotics. With the gastroscope the stoma in gastro-enterostomies is well seen, and the following conditions have been observed in many cases: marginal or jejunal ulcers, all forms of gastritis, the presence of silk sutures acting as a foreign body, and recurrent or new carcinoma of the stoma.

GASTRIC ULCER

True gastric ulcer can usually be well seen through the gastroscope. However, when the ulcer occurs on the lesser curvature of the antrum it is then hidden from view by the angulus. The picture of the ulcer is striking. The edge is sharp, with an abrupt transition between the ulcer and the normal mucosa. The ulcer may be round or oval, and the base has a brilliant yellowish white or yellow color. Occasionally, in an ulcer which is bleeding or oozing, the base may be red. It is important to note at this point that Schindler has observed over 100 true chronic gastric ulcers, and has never observed one to become malignant. The development of the true gastric ulcer is still not definitely understood. However, a frequent accompaniment of ulcer is hemorrhagic spots, usually seen along the lesser curvature. These spots seem to appear within 6 months after the development of an ulcer and in patients who later develop ulcer. Whether they have something to do with the formation of the true gastric ulcer is still uncertain. They have never been found in cases of anacidity. Schindler has observed cases with hemorrhagic spots which later developed true chronic gastric ulcers, and is of the opinion that there is a definite connection between them. This opinion is not accepted by Faber, Konjetzny, and Hurst, who maintain that a true gastric ulcer arises from gastritis or a preceding irritation.

The question may be raised as to the danger of gastroscoping patients who have recently had a hemorrhage. The answer is based upon the experience of thousands of gastroscopies, which have been performed under these conditions by the leading men in this field, without any complications. It has been proven that inflation of a small amount of air will not cause bleeding. As previously stated, movement is rarely observed in the body of the stomach during the examination. It is desirable and valuable to do gastroscopy after hemorrhage, as the condition found may be ulcer, soft polyp, or other conditions in which the true nature and site of the bleeding is important to know. Subsequent treatment depends much upon this information.

TUMORS

Benign tumors are commonly found gastroscopically, but are rather difficult to demonstrate with X-ray, even with the most refined technic. They may be either single or multiple, and frequently have a stalactite or stalagmite formation. There is no doubt that gastric carcinoma can develop from these tumors, and observation of this transition is possible gastroscopically. I have previously called attention to the fact that they have been frequently observed in chronic atrophic gastritis.

GASTRIC CARCINOMA

Gastroscopy can aid greatly in the diagnosis and determination of operability of gastric carcinoma. When ulcerated, the lesion has the following characteristics: One edge is usually limited, but the other edge shows a gradual transition of the process from the floor of the lesion to the surrounding mucosa. The edge is irregular and the base has a dark brown or violet color. The diffusely infiltrating lesions are seen in varying degrees of shape, size and color. The extent of the involvement can often only be determined by the gastroscopic appearance.

We are all aware of the high mortality in gastric carcinoma and the importance of its early diagnosis. In this way only can we hope to cope with this disease. It is well to emphasize again certain cardinal features, such as unexplained loss of weight, anorexia, and weakness, as signals demanding the most exacting investigation. This means particularly the correlation of roentgenologic with gastroscopic studies. I am furthermore convinced that it is the gastroenterologists who will continue to sustain the enthusiasm and interest so necessary for the scientific advancement of this subject.

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Urea: Its Use In Infections.—In 1923 the writer reported a series of 31 cases of osteomyelitis affecting various bones of the body, and in 5 of which he was able to trace, chronic recurrent lesions developed. The mode of treatment followed was surgical incision and drainage. Some were treated with the Dakin solution technic and some by simple saucerization and drainage. In the early cases good results were obtained in about 6 weeks, but it seemed that once a case went beyond that period it became chronic and necessitated further operative procedures. . . .

William Robinson reported that allantoin, which occurs in maggot excretions, affected the healing of wounds of indolent or chronic character. It was found by him that urea, which is also present in maggot excretion, has similar effects to allantoin. The urea has an extremely wide distribution and may be prepared synthetically. He reported in collaboration with many physicians, various infections treated with 2 per cent urea solution. The solution is bland, stable and nontoxic, and apparently has no ill effects upon the surrounding tissue. It is not an antiseptic, for germs can be easily conveyed in a strong solution of urea. It is easily soluble in distilled water and does not seem to possess proteolytic properties. . . .

Summary.—Eight cases were presented in which the use of urea, according to the method outlined by Robinson were presented. The use of pure crystals has been resorted to in very indolent cases with apparently good results. There were 2 failures not reported above, but which could not be blamed on the solution, as both of these cases were in which sinus leading to osteomyelitic processes, and which have not been freshly operated on. Both of these patients were advised to have a saucerization operation with subsequent treatment.

It seems reasonable to assume that a new and very potent factor in the healing of indolent wounds has been added to the armamentarium of the surgeon.

Extract from article by Leon M. Bogart, M.D. Flint, Michigan, *Journal, Michigan State Medical Society, May, 1937*, p. 285.

THE INDICATIONS FOR PRESACRAL SYMPATHECTOMY FOR VESICAL CONDITIONS

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It is singular that surgery of the autonomic nervous system created so little interest until recent years. Only during the last decade has any general interest been manifested, although some of the physiological activities, such as Horner's syndrome, sweating, vasodilatation, secretions of some of the glands, and the pain of angina pectoris have been known for some time to be dependent upon the autonomic nervous system. The indications for surgery in this field depend upon a physiological basis; there is usually present no pathological lesion which can be excised and examined microscopically, although Crile thinks that the celiac ganglia excised from those patients suffering with severe hypertension are increased in size and weight, and show hyperplasia. Advancement in the knowledge of neurophysiology during the last few years has furnished data which establish some surgical procedures on the autonomic nervous system as logical, and clinical results have demonstrated their merits. There is much yet to be known about neurophysiology, and a few operations such as celiac ganglionectomy for hypertension must be considered as experimental at present.

One must know the neuro-anatomy and neurophysiology of the affected region of the body before he can deal with the problem surgically with intelligence. Also, he should have reasons to believe that the altered physiological changes produced by surgery shall be advantageous; and he should have had the clinical experience to know that the desired results are usually produced before he can conscientiously recommend the operation to his associates or to the patient. Fortunately a sufficient knowledge of the anatomy and the physiologic activities of the presacral nerve (superior hypogastric plexus) has been attained to allow intelligent discussion of the operation of presacral sympathectomy, and the clinical results have been observed on many patients.

Craig has discussed the development of presacral sympathectomy. I have previously described the anatomy of the presacral nerve (superior hypogastric plexus), a description which was based on the studies of Learmonth and Elaut. It belongs to the sympathetic nervous system and it is situated in the iliac trigone of Elaut. It is always prelumbar and consists of a single nerve in 24 per cent of the patients and of some type of plexus in 76 per cent. It is connected with the celiac ganglia by a central preganglionic root which constitutes about 40 per cent of the nerve or plexus. Each lateral root consists of postganglionic medullated fibers and is formed by branches from the first and second lumbar ganglia respectively. Additional communications are received from the third and fourth lumbar ganglia on each side. The presacral nerve (superior hypogastric plexus) divides into two hypogastric branches at the level of the promontory of the sacrum. Each branch follows the general course of the iliac vessels on each side and ends in the respective inferior hypogastric ganglion.

The parasympathetic nerves to the bladder are detached from the anterior primary divisions of the second, third, and fourth sacral nerves and gain the lateral aspect of the hypogastric ganglia. The somatic nerves of the bladder are derived from the anterior primary divisions of the third and fourth sacral nerves.

Learmonth operated on patients under low spinal anesthesia and observed, in coöperation with a cystoscopist, that when the distal end of the divided nerve or plexus was stimulated with a faradic current, there was contraction of the ureterovesical sphincters, the internal sphincter, and the trigone, and of the musculature of the prostate gland, seminal vesicles, and the ejaculatory ducts. The blood vessels of the mucosa dilated. Stimulation of the central end of the divided nerve or plexus caused the patient to experience the sensation of a "crushing pain" referred to the bladder. Learmonth also observed the inhibitory effects of the sympathetic nervous system in the human subject by manometric recording of increased bladder capacity after administering adrenalin intravenously. Head and Riddoch, and again Foulds observed that after interruption of the sympathetic fibers to the bladder, the normal suprapubic pain of overdistention of the viscus did not occur.

The parasympathetic nerves furnish the motor fibers to the detrusor muscle, the sensory fibers to the vesical mucosa, and the micturition reflex.

Ostensibly presacral sympathectomy for a vesical disorder would be indicated only when relief or improvement could be expected by effecting any one, or a combination, or all of the following conditions:

1. Relaxation of the ureterovesical orifices.
2. Eliminating the crushing type of pain of muscular contraction.
3. Production of vasodilatation.
4. Removing the inhibitory influence to the emptying nerves of the bladder.
5. Relaxation of the trigone and internal sphincter.
6. Paralysis of the musculature of the prostate gland, seminal vesicles, and the ejaculatory ducts.

When one performs a presacral sympathectomy he makes a paramedian subumbilical incision. The patient is then placed in the Trendelenburg position. The small intestines are packed upward and to the right, and the sigmoid is retracted to the left. A longitudinal incision about 3 cm. long is made in the posterior parietal peritoneum just over the promontory of the sacrum. Search for the nerve fibers is begun with the right iliac artery and continued over to the left iliac vein. As the nerve fibers are encountered they are collected on a hook. The right ureter is attached to the peritoneum, and the middle sacral artery is located in a deeper plane; consequently, these should cause no trouble. About 3 centimeters of the nerve or fibers are excised, requiring no ligatures. The posterior parietal peritoneum is then closed with continuous catgut suture, and the anterior abdominal wall is closed without drains in the usual manner.

Ward has performed presacral sympathectomy on a patient suffering with hydroureters with fairly good results. When the hydroureters are resulting from a spastic condition of the ureterovesical orifices, one may expect excellent results from this operation. However, dilatations should always be tried first. One may attain some idea of the results of this operation on a patient beforehand by giving him neo-iopax intravenously and studying the ureters by fluoroscopy. After he has observed the ureterovesical orifices in this manner, he gives the patient 0.15 Gm. of acetyl choline intramuscularly and continues the fluoroscopic study for a period of 15 minutes. If the emptying of the ureters is improved and the ureterovesical orifices become more patent, one can be fairly sure that interrupting the sympathetic fibers will produce favorable results.

Learmonth, Douglass, McConnell, and Quinby have all performed presacral sympathectomy on patients suffering with severe interstitial cystitis. Their reports show that most of the patients experienced some relief of pain but that few were completely relieved. However, the cystitis improved very rapidly in most cases because of the increased circulation of the bladder resulting from the vasodilatation. That part of the distress which could be interpreted as caused by muscular contraction and ischemia of the vesical wall disappeared. In my experience the operation is indicated on those patients suffering with intractable cystitis who have failed to secure relief by other types of therapy.

This operation should rarely be done on patients who are suffering with inoperable malignant lesions of the bladder. Learmonth, McConnell, and others have reported that the patient does receive some relief from pain. Since the afferent fibers to the vesical mucosa are furnished by the parasympathetic nervous system and since a malignant neoplasm always involves the mucosa, the rationale of the operation is questionable. Few of these patients will dispense with narcotics after the operation.

The operation has given greatest relief to those patients who are suffering with the so-called cord bladder of nonluetic origin. In this group there exists an imbalance between the sympathetic and the parasympathetic nervous systems. It appears that the "braking effects" of the sympathetic nervous system overbalance the impulses to the detrusor muscle. If the parasympathetic nerves are entirely eliminated the operation is not warranted. For this reason it is contraindicated for those patients suffering with a luetic cord bladder unless one is sure that the syphilitic infection has been arrested before complete destruction of the motor fibers has occurred. It is also contraindicated in those patients who are suffering with physiological or anatomical severence of the spinal cord. Results have been most gratifying among those who have received injury to the spinal cord without complete severence, those who have had tumors or anomalies of the cauda equina or that region of the spinal column and after removal suffer from residual damage, and those who have recovered from intracranial accidents or surgical operation with residual damage, or the imbalance may be idiopathic. I have done many operations on patients belonging to this group and in some the results have been most brilliant. Usually it will require several weeks for the residual urine to disappear. Immediately following the operation an indwelling catheter is placed in the bladder and the patient is given 0.10 Gm. of acetyl choline intramuscularly twice daily. This régime is continued for 14 days, by which time the patient is ambulatory and the catheter is removed. He is instructed to attempt to void while in a sitting position once each hour during the day and once every 2 hours during the night. His residual urine is determined at least once daily. By the end of 3 or 4 weeks the residual urine will have diminished to about 10 to 15 cc., and this quantity becomes constant due to the paralysis of the trigone. The patient must be told to attempt to void once every hour during the day, because the micturition reflex has been ignored for so long that it no longer registers, and it appears again only after training. Likewise, due to the prolonged distention of the bladder, it requires several weeks for it to regain its muscular tonus. Finally the micturition reflex and the tonus will become normal. The cystometric measurements may or may not become normal depending upon the status of the emptying nerves of the bladder.

I have performed a presacral sympathectomy on a male patient 19 years of age, who was suffering with nocturnal enuresis. Cystoscopic examination revealed a large bladder with a capacity of 700 cc., and the internal sphincter and the trigone appeared spastic. It was thought that this spastic condition of the sphincter prevented complete emptying of the bladder during the day and that when he fell asleep it became relaxed, a condition which permitted enuresis. A presacral sympathectomy was performed and the patient was completely relieved of his trouble.

Paralysis of the musculature of the prostate gland, seminal vesicles, and ejaculatory ducts, which is one of the results following presacral sympathectomy, appears to have no clinical application. Rather it is an undesirable sequel. After this operation the male patient will experience psychic orgasm but he will not ejaculate. His sexual potency is usually increased but he may be sterile. This information should be imparted to the male patient beforehand.

Conclusion

Presacral sympathectomy is indicated for patients who are suffering with hydro-ureters caused by spasticity of the ureterovesical orifices after other methods of therapy have failed to effect relief, for patients who are suffering with nonluetic cord bladders in whom a true imbalance exists between the inhibitor nerves and the emptying nerves, and for patients suffering with nocturnal enuresis associated with increased bladder capacity and spasticity of the internal sphincter.

The operation has a limited application to patients who are suffering with intractable interstitial cystitis. It eliminates some of the pain and increases markedly the blood supply to the vesical mucosa by producing vasodilatation which aids greatly to combat the disease. It is rarely indicated for patients who are suffering with inoperable cancer of the bladder. It should not be performed on those patients suffering with luetic cord bladders or on anyone if the parasympathetic nerves have been destroyed by any cause. The chief objectionable feature to the operation is that the male patient is frequently rendered sterile. He does not become impotent.

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The Galactose Tolerance and Urobilinogen Tests in the Differential Diagnosis of Painless Jaundice.—We do not propose to go far into the large and confusing field of liver function tests, but wish simply to describe our results with the galactose tolerance and urobilinogen tests in 80 consecutive cases of painless jaundice in order to evaluate how much they have helped in diagnosis.

By painless jaundice we mean cases of jaundice without pain or in which pain was a mild or minor symptom. The group consists of 17 cases of acute infectious hepatitis (catarrhal jaundice), 17 cases of acute toxic hepatitis, 12 cases of obstruction of the common bile duct and 34 chronic intrahepatic cases, mostly cirrhoses, with an acute exacerbation of jaundice....

Summary.—The urobilinogen and galactose tolerance tests in the urine were used in 80 cases of painless jaundice in the medical wards.

The tests were positive, as a rule, where diffuse liver-cell damage predominated, as in catarrhal jaundice and toxic hepatitis. A positive galactose test in painless jaundice (with diabetes ruled out) points to liver degeneration, and the excretion of large amounts (6 to 7 gm.) is practically conclusive. The tests were negative, as a rule, where there was malignant obstruction of the common bile duct. In painless jaundice the important diagnosis is to distinguish between the medical and surgical types. This is especially true in middle life when cancer is frequent. The combination of these two simple tests has proved a useful aid in distinguishing several groups of medical and surgical cases, namely acute and chronic, toxic and infectious hepatitis from painless obstruction outside the liver.

One of the most important findings was the persistent absence of urobilinogen in obstructive jaundice due to cancer of the head of the pancreas or common bile duct. Persistent acholia of the stools, developing rather early after 2 or 3 weeks of jaundice, with persistent absence of urobilinogen in the urine appears to be the rule in malignant obstruction and rarely occurs in other forms of jaundice. In acute hepatitis the absence of urobilinogen is only temporary, and in the obstruction due to stone is rarely complete. In our 1 case of silent stone in the common duct, the *constantly increased* urobilinogen was in sharp contrast to its *persistent absence* in the 10 cases of malignant obstruction.

In gallbladder cases, which are often surgical, the tests were usually not distinctive. They depended, apparently, on the amount of associated hepatitis or infection and resembled those in the medical cases of acute and chronic hepatitis, and the diagnosis was made from other clinical data. Occasionally there may be great difficulty in distinguishing painless *partial* obstruction of the common bile duct with secondary damage to the liver from a primary subacute or chronic, diffuse disease of the liver. This occurred once in our series.

On account of the variation in liver function at different periods of an attack of jaundice and because of some variation in the tests themselves, it is not wise to base diagnosis on a single test. A course of tests, beginning early, if possible, and carried through the height of the jaundice for a week or two, is far more valuable.

A positive galactose test in painless jaundice indicates liver degeneration; a normal test does not always exclude liver-cell injury. The urobilinogen test has value in showing the presence or absence of bile in the bowel, as well as being a very sensitive indicator of liver disturbance. It is a more definite guide to liver dysfunction than the galactose test, if hemolytic jaundice is excluded, and is more often useful in distinguishing intrahepatic from external obstructive jaundice; but a combination of the two tests is best of all.

The tests have a definite value in prognosis by measuring the speed and degree of recovery of liver function after an attack of jaundice. The urobilinogen and galactose tests may remain positive long after active symptoms have disappeared, thus showing residual liver damage. In an occasional borderline case, the tests may be inconclusive or even misleading. Finally, these simple tests have proven useful aids and have definitely improved our differential diagnosis of painless jaundice. They deserve to be used more widely in this particular field.

Extract from abstract by Franklin W. White, M.D., Boston, *New England Journal of Medicine, June 10, 1937, p. 1,017.*

A CASE OF BETA-HEMOLYTIC STREPTOCOCCIC INFECTION TREATED WITH PARA-AMINO-BENZENE-SULFONAMIDE*

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If 2 years ago some therapeutic enthusiast had predicted that tablets intended for oral administration, containing a comparatively simple coal-tar derivative, would shortly be available as a specific treatment for even the most serious types of hemolytic streptococcic infections, including septicemia and peritonitis, he would properly have been accused of letting his enthusiasm outrun his judgment. Had he added that this therapeutic success would mark the inauguration of a new epoch in the chemotherapy of infectious disease his sanity would probably have been put in question. Yet today a rapidly accumulating mass of clinical evidence vigorously supports the former contention and justifies entertaining a rational hope of the truth of the latter. This is neither the time nor the place for any comprehensive review of the development of this method of treatment nor of the animal experimentation on which it is based, even if my knowledge of chemistry and bacteriology were equal to the task. It is only proposed to present here sufficient data to make the nature of the treatment understandable and then to report a case in which its employment was apparently attended with phenomenal results.

Two years ago this month (February, 1935) Domagk reported that through the use of a derivative of para-amino-benzene-sulfonamide he was able to save the lives of mice in which streptococcic peritonitis had been experimentally produced. This observation has been confirmed by all subsequent investigators. Isolated employment of the drug in the treatment of human streptococcic infections by several European clinicians followed immediately, but the results reported seem to have received little notice until Colebrook and his associates, in June, 1936, published their findings in the treatment of 38 cases of this type of puerperal infection at Queen Charlotte's Hospital, in London. In December of the same year an additional 26 cases were reported from the same clinic, thus making a series of 64 cases of streptococcic puerperal infection treated by this method. In these 64 cases the mortality rate was 4.7 per cent as against an average mortality of 22.8 per cent in 495 cases observed at the same hospital in the years 1931 to 1935, inclusive. The startling nature of some of their results is well illustrated by the following case report:

> "Mrs. S., primipara, developed fever to 105°F. on the third day, and on admission was very gravely ill. Blood culture gave a growth of more than 5,000 colonies per cubic centimeter on the first 2 days, and over 3,000 on the third day, most, if not all, of the colonies being hemolytic streptococci although there were also some anaerobic streptococci in fluid cultures made at the same time.
>
> "On the fourth day of treatment a blood culture was sterile and the temperature fell to normal, remaining so except for 1 slight rise (to 100°F.) the next day. The woman was discharged in good health 21 days after admission and suffered no relapse."

On this case the authors make the following comment:

> "In view of the fact that blood cultures yielding such a large number of hemolytic streptococci (equivalent to something like 30,000,000 in the whole blood stream) have never previously been observed by the authors except in the terminal stages of a fatal infection, this patient's prompt recovery was astonishing."

In America, Long and Bliss of Johns Hopkins Hospital seem to have been the first to appreciate the importance of the results being obtained at Queen Charlotte's Hospital, and in the summer of 1936 they undertook an experimental and clinical study of the subject themselves. In January, 1937, in a preliminary communication giving the bibliography to date and admirably summarizing present knowledge of the subject from the chemical, bacteriological and clinical points of view, they, in the main, confirmed the previous experimental findings and from the clinical standpoint reported treating 19 cases of various kinds of streptococcic infection, many of the patients being desperately ill, with only 2 deaths. In an as yet unpublished paper read before the Washington Gynecological Society in January, 1937, Long stated that they had had 4 cures in 5 cases of streptococcic meningitis, that their results in treating meningococcic meningitis had been as good, if not better, than those obtained from the employment of the best available anti-meningococcic serum, and that there was even some evidence that the drug exerted a beneficial action in pneumonia due to certain types of pneumococcus. Results such as these from such responsible sources can only be characterized as revolutionary, and add point to some brief consideration of the chemical formulae of the drugs employed, the mechanism of their effect on the streptococcus in vivo and in vitro, and their dosage and method of clinical use.

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* Read before the Clinico-Pathological Society, February 16, 1937.

The base substance, now obtainable in tablet form, is para-amino-benzene-sulfonamide, the therapeutic effect of which, and of 2 of its derivatives, has been studied experimentally and clinically. These 2 derivatives are: (1) The hydrochloride of 4′-sulfamido-2, 4 diamino-azo-benzene, obtainable in tablet form under the trade name of Prontosil Tablets; and (2) a 2.5 per cent aqueous solution of the disodium salt of 4′-sulfamido-phenyl-2-azo-7-acetylamino-1-hydroxynaphthalene-3, 6-disulfonic acid, a red dye resembling exactly red ink and marketed in 5 and 10 cc. ampules under the trade name of Prontosil. For obvious reasons correct medical literary style to the contrary notwithstanding, these drugs will be subsequently referred to by their short trade names.

The exact nature of the mechanism through which the drugs deleteriously affect the streptococcus is still unknown and those who have most studied this point are not in entire agreement. From in vitro experiments it seems definitely established that the presence of the dye, Prontosil, in various dilutions, is without effect in inhibiting the growth of streptococci in different culture media. It is believed that Prontosil is broken down in the body into the parent substance, Prontylin, and that it is the concentration of this chemical in the blood and tissues that produces the therapeutic effect. Since this substance is readily absorbed from the stomach, the clinical use of "Prontosil" has been discontinued by Long and he administers Prontylin orally except in cases where because of vomiting, coma, or for other reasons, parenteral administration is indicated. It also seems to be definitely established that Prontylin, that is, para-amino-benzene-sulfonamide, in various concentrations in both broth cultures and in 50 per cent normal horse serum broth, does exert a definite effect in retarding the growth of streptococci. In this connection the following findings of Long and Bliss may prove to be of great significance. They say:

> "It is also interesting to note that a 1:10,000 concentration of para-amino-benzene-sulfonamide in serum broth markedly inhibited the growth of alpha hemolytic streptococci, gamma streptococci, pneumococcus types I and II, several varieties of Neisseriae from the throat, Micrococcus tetragenus, Haemophilus influenzae and Haemophilus haemolyticus. The growth of Staphylococcus aureus, typhoid bacilli, para A, para B, enteritidis, Flexner, Shiga and several other gram-negative bacilli was not affected by this concentration of the chemical."

What is the significance of this apparent resistance of gram-negative organisms to the drug? It also seems to be definitely established that concentration of Prontylin in the blood stream stimulates phagocytosis, but as to whether this is due to activation of the leukocytes or to sensitization of the streptococci is still a matter for conjecture. On the other hand, Colebrook, in his recent address at Walter Reed General Hospital, states that if the cellular content of blood from an individual ingesting Prontylin were transferred to normal human serum the resulting mixture was without effect on streptococci; if, however, cells from normal blood were transferred to Prontylinized serum the mixture was still effective. The significance of this finding, if confirmed, remains to be determined.

The dye Prontosil is usually given intramuscularly, although it is as rapidly absorbed when given subcutaneously and does not result in unpleasant local reactions. Prontylin is administered perorally. Both drugs are usually given synchronously, Prontosil for a 24-hour period, after which it is discontinued and the treatment continued with Prontylin. The dosage advocated by Colebrook is as follows:

Severity	By Mouth	By Intramuscular Injection
Gravely ill patients.	12 tablets per day	20 cc. every 8 hours
Cases of moderate severity.........	6 tablets per day	20 cc. every 8 hours
Mild cases.........	6 tablets per day	10 or 20 cc. twice daily

Long advocates larger doses. In severe cases, when necessary to use Prontosil, he gives it in a total 24-hour dose equivalent to 1 cc. per pound of body weight, one sixth of the total being administered subcutaneously every 4 hours. The treatment is then continued with Prontylin perorally at 4-hour intervals, the total daily dose seldom exceeding 5 Gm.

The drugs seem to have an extraordinarily low toxicity. Large doses of Prontosil turn the patient a uniform pink and the urine is tinted red; this coloration rapidly fades. There has been occasional evidence of a mild and transitory renal irritation that seems to be negligible. Sulphemoglobinemia has occurred in several cases, according to Colebrook in patients to whom magnesium sulphate has been given, but this, also, seems to be transitory and negligible, since it promptly disappears when the dosage is lowered or the drugs discontinued. In some cases a decided lowering of the CO_2 combining power of the blood evidences an acidosis. It is still too soon to know whether the treatment is attended with any danger of the development of late sequelae, but such a possibility must be borne in mind. None such seems to have been reported so far.

In view of all of these clinical findings it is hoped that a report of a case of streptococcic infection treated by this method may not be without interest.

Report of Case

Mrs. D. D., a 31-year old primigravida, first consulted me on May 15, 1936, referred by Dr. Fred L. Adair, of Chicago. Confinement was estimated for December 16, 1936. The anamnesis was essentially negative. The patient stated, however, that for some time past she had been running a low-grade fever in the late afternoons, and she was referred to Dr. Worth B. Daniels for study from this angle. The findings of his general physical examination were essentially negative. A hemogram showed 76 per cent hemoglobin; erythrocytes numbered 4,290,000 per cu. mm., and leukocytes 11,000, with 70 per cent polymorphonuclear neutrophiles and 7 per cent band forms. Urinalysis was entirely normal. The Kahn test of the blood was negative. The following examinations were made at the National Institute of Health: Agglutination tests for Brucellosis—negative; B. tularense—complete agglutination 1:10 only. A tuberculin test (intradermal) was positive. X-ray report by Dr. A. C. Christie, May 22, 1936, read: "Examination of the chest shows increased density at the roots of both lungs and along the main bronchial trunks to the lower lobes. The appearance is that of a nontuberculous hilum infection, such as is often associated with inflammatory disease of the upper respiratory tract, especially disease of the nasal accessory sinuses. There is no evidence of disease of the lung parenchyma." The temperature chart over a period of 1 week showed a varying rise of temperature as high as 99.6°F. but usually 99°F. to 99.3°F. almost every day. Nose and throat examination by Dr. G. H. Mankin showed minimal involvement of the ethmoid sinuses. He felt that in the absence of any other ascertainable cause of low-grade fever it is possible that this might be causing it. He directed the patient as to treatment.

The course of the pregnancy was entirely uneventful with exception that a considerable hydramnios developed in the last few weeks, and the low-grade fever continued at intervals.

Labor was initiated spontaneously on November 27, 1936, 3 weeks before term; due to the hydramnios there was a primary inertia, and it was terminated by mid-forceps delivery and episiotomy in 14 hours. The baby was abnormal and died in 6 hours.

At the end of the third postpartum day the temperature rose for the first time to 99.8°F. and the pulse rate to 100. From this time through the fifteenth postpartum day the course of the disease was as follows: The temperature remitted on only 4 occasions below 101°F., with the daily peak after the first few days usually between 103°F. and 104°F. On the eleventh day the peak was 105.5°F. and on the fourteenth, following a transfusion, 107.2°F. The pulse ranged from 80 to 130, mostly between 100 and 120. Appetite was fairly well maintained and the patient took fluids well, but there were frequent chills and she was slightly irrational at times and quite apprehensive throughout. On the sixth day there was much complaint of pain in the rectum; on the following day purulent drainage from the perineal wound was noted, and it was hoped that this local condition was responsible for the general one. The leukocyte count ran as follows: fourth day, 12,200; ninth, 10,000; eleventh, 13,000. The differential leukocyte count on the ninth day showed: bands, 4 per cent; polymorphonuclears, 83 per cent; lymphocytes, 13 per cent; hemoglobin, 75 to 78 per cent (3 readings during this period). The urine contained traces of albumin and a few epithelial cells and leukocytes. On the thirteenth day a blood culture was taken, and on the fifteenth day Dr. Tomas Cajigas reported: "Blood culture shows streptococcus hemolyticus, moderate growth."

On the following day, the sixteenth postpartum day and thirteenth day of fever, my attention was called to the new treatment of streptococcic infections with Prontosil, and this method of therapy was discussed with the family. It developed at this time that the patient's mother died about a year previously from a streptococcic infection following a gallbladder operation, and her husband's cousin from a streptococcic sore throat 7 months previously. The patient had been exposed to both of these cases. In view of these circumstances the husband naturally adopted a fatalistic attitude toward the situation and expressed the desire that his wife should not be tortured, as he expressed it, with frequent transfusions and serum therapy which had proved to be so futile within his recent experience. He did, however, agree to a trial of the Prontosil.

This was administered, according to the directions contained in the package, in 5 cc. doses intramuscularly every 4 hours, beginning at 2 P.M. on the sixteenth postpartum day. This dosage was continued for 24 hours. No marked change in the patient's condition was noted, although the temperature failed to fluctuate and maintained itself between 102.8°F. and 103.6°F. Following telephonic consultation with Dr. Perrin H. Long, in Baltimore, at 6 P.M. on the following day, the seventeenth postpartum, subcutaneous injections of Prontosil in 25 cc. doses, at 4-hour intervals, were begun, together with 1 Gm. (4 tablets) of Prontylin perorally at the same intervals. By 12 midnight the temperature had dropped to 101°F., reached 99.4°F. the following morning, reacted to 101°F. in the afternoon, and the next morning registered 97.8°F., at which time the pulse, which had been running around 128, had dropped to 88. On this day, the second after the initiation of this massive dosage, the temperature remained below 98.4°F. The following day it reached 99.2°F., and the next day 100.2°F., and this proved to be the initiation of a mild febrile reaction of 7 days' duration, the maximum temperature being 101.8°F., due to the development of a phlebitis in the left leg. The temperature again reached normal on the twenty-eighth day postpartum and remained there during the balance of the patient's hospitalization.

Altogether the patient received 180 cc. of Prontosil, 30 cc. in the first 24 hours of its administration and 150 cc. in the second. Following the discontinuance of the Prontosil the dose of Prontylin was increased from 6 to 8 Gm. daily and maintained at this level for 2 days. On the twentieth postpartum day it was reduced again to 6 Gm., on the twenty-fifth day to 4 Gm., and on the thirty-third day to 2 Gm., and finally discontinued on the thirty-ninth day. A blood culture started on the seventeenth day, which was the day of massive dosage, showed a scanty growth of streptococcus; the result of the culture on the following day was the same, but the next 2 daily cultures were negative. On the day of massive dosage the urine showed a heavy trace of albumin but was negative thereafter. The leukocyte count on the day of massive dosage was 20,150 with 11 per cent band forms and 82 per cent polymorphonuclears. Two days later the leukocytes had dropped to 15,150, with 12 per cent band forms and 75 per cent polymorphonuclears; and 4 days later the leukocyte count was 15,600, with 1 per cent young forms, 12 per cent band forms, and 60 per cent polymorphonuclears.

From these massive doses of drugs, aside from the effect on the temperature and pulse and the immediate improvement in the general condition, 4 developments were noted: the urine was colored red; the skin, mucous membrane and conjunctivae were uniformly colored pink; there was an extensive maculopapular eruption covering the buttocks and the back; and there was marked cyanosis of the lips and finger tips. All of these symptoms rapidly disappeared with the discontinuance of the Prontosil.

The recovery of the patient has been complete with the exception of some slight but persistent swelling in the left leg. Postpartum examination on February 5, 1937, slightly over 2 months following the beginning of the infection, disclosed no pelvic disease.

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The Effect of Pilocarpine on Neurogenic Urinary Retention.—The relation of urinary tract infections to repeated catheterizations in cases of retention is well known. The employment of some drug which might eliminate the necessity of catheterization in such cases would be ideal from the standpoint of convenience as well as that of the prevention of infection.

Many investigators have reported on the therapeutic employment of autonomic drugs in cases of neurogenic vesical dysfunction. The majority of reports have been regarding patients in whom there were bladder disturbances after operation and in whom there was no gross neurological lesion. This paper contains the results of a study of a series of cases in which the vesical symptoms were due to disease of the nervous system. . . .

Conclusions.—That pilocarpine possesses a therapeutic action in retention is shown by several facts: (1) In 17 of 19 patients with retention, micturition occurred after treatment; (2) the patients usually voided within 45 minutes after the injection of pilocarpine, and 2 cases voided *only* after the drug; (3) of the 17 patients who responded to the drug, 12 regained micturition within 24 hours after commencement of injections; (4) in approximately one half the cases "abstinence retention" occurred when medication was stopped (15 cases so studied); (5) urgency was experienced within 45 minutes after the injection by 15 of the 19 patients; (6) residual urines were substantially decreased in 7 of 8 patients.

Pilocarpine appears to have definite value, and its reasonably prolonged administration is unattended by toxic effects of any serious consequence.

Summary.—1. A résumé of current conceptions regarding the neurophysiology of the urinary bladder is presented. The parasympathetic division of the autonomic nervous system is concerned with the expulsion of urine from the bladder; the sympathetic, with the retention and accommodation of urine in the bladder. The motor function of the parasympathetic vesical innervation appears to be considerably more dependent upon the function of upper or suprasegmental motor neuron than is the sympathetic.

2. Of 19 cases of urinary retention, 17 responded to pilocarpine therapy by micturition, and in 15 cases catheterization was eliminated.

3. In cases of neurogenic urinary retention, urgency and the accomplishment of micturition are considerably facilitated by the administration of pilocarpine.

Extract from article by James S. Dean, M.D., New York City, *Bulletin, Neurological Institute of New York, January, 1937, p. 154.*

ARTERIAL HYPOTENSION

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It is surprising how frequently conditions are encountered in which low blood pressure appears to be one of the chief symptoms, or even the only outstanding feature. The small amount of space devoted to discussions of arterial hypotension in most text-books would seem to indicate that this is an unusual and unimportant condition. And yet surveys by Barach, Alvarez, and others show that hypotension, i.e., a systolic pressure less than 110 mm., Hg., occurs in at least 2 to 3 per cent of all individuals. A review of my own records reveals no less than 54 cases in which a systolic pressure of less than 110 mm., Hg., was detected. In 36 of these the systolic pressure was less than 100 mm., Hg.

Of course, it is realized that low blood pressure does not necessarily represent a pathological condition and in many instances may be compatible with perfect health. It is also true that hypotension should usually be considered as a symptom of some diseased condition, rather than as a disease in itself. On the other hand, it seems to be generally agreed that such a condition as essential hypotension does exist. Furthermore, it is evident that in many conditions in which there is an associated hypotension, the latter is itself responsible for certain important subjective symptoms.

Despite the high incidence and apparent importance of low blood pressure, one may search in vain for any thorough discussion of the subject in the usual text-books. No mention is made of hypotension in Cecil's "Text-book of Medicine." Lewis, in his "Diseases of the Heart," devotes an entire chapter to hypertension but says nothing at all about hypotension. Stevens includes only 18 lines on the treatment of hypotension in his "Text-book of Therapeutics," and 11 additional lines on treatment can be found in Osborne and Fishbein's "Handbook of Therapy," while no mention of the subject is made in Beckman's "Treatment in General Practice." Cabot's "Physical Diagnosis" dismisses the subject with the following remarks:

> "Excellent health is often associated with abnormally low blood-pressure readings. We seldom get much help from them. The lowest readings occur in Addison's disease (even to 50 mm.), after hemorrhage, infectious fevers (tuberculosis, pneumonia, typhoid) and surgical 'shock.' Occasionally attacks of faintness, vertigo, headache and muscular debility are associated (especially in young adults) with a hypotension of unknown origin."

Concerning the pathological changes involved, MacCallum is even less helpful. His complete discussion of the subject is as follows:

> "The admirable mechanism which maintains the flow of blood at optimum rate, volume, and pressure, and reëstablishes these optimum conditions very rapidly when they are disturbed by some unusual exertion or otherwise, is itself sometimes disturbed so that it cannot keep its control. Then we may have the blood circulating under abnormally low or abnormally high pressure (hypo- and hypertension). The rate and volume of the blood flow are not so easily measured as the pressure, and it may be said at once that the causes of such changes are, for the most part, unknown, although there are many theories."

MacCallum offers no explanation of the mechanism which maintains normal blood pressure. However, a consideration of this mechanism is necessary in order to understand how hypotension develops. Friedlander states that the factors which maintain blood pressure are:

1. The force of the cardiac contraction.
2. The condition of the vessel walls.
3. The peripheral resistance to the blood stream, determined by the vasomotor system.
4. The blood volume, and the physical state of the blood itself, its viscosity, etc.

Friedlander asserts that these factors are not of equal importance. It is obvious that if the myocardium becomes inefficient from any cause, so that it contracts feebly or inefficiently, the blood pressure will fall. This occurs usually, however, only in the terminal stages of myocardial degeneration, in occasional cases of paroxysmal tachycardia, and rarely in heart block.

The physical state of the conducting vascular system probably plays an important part in the production of hypotension associated with acute infectious diseases. In these conditions, flaccid and toneless muscle fibers in the blood-vessel walls subsequent to the toxemia may temporarily cause the blood pressure to be lower.

Peripheral resistance is perhaps the most important single factor, both in the maintenance of normal pressure and in the production of hypotension. The arterioles and capillaries are held normally in a state of tonic contraction by impulses delivered from the vasomotor center. Peripheral constriction is thus subject to the ebb and flow of vasomotor impulses. The endocrine system coöperates with the vasomotor system, exerting either a pressor or depressor action on vasomotor function. Endocrine dysfunction, therefore, plays a definite part in the production of hypotension.

The fourth factor, change in the blood volume, is of considerable importance in the production of certain types of acute hypotension, namely, traumatic, posthemorrhagic, and "shock" hypotension. The usually mild hypotension associated with anemia may be due in part to the diminished viscosity of the blood resulting from the lowered cell count.

Low blood pressure is associated with such a large number of unrelated conditions that it is practically impossible to present a complete classification of the causes. The enumeration of some of these causes will, however, serve to demonstrate the frequency of the condition.

Hypotension may be divided into 2 types, namely, acute or temporary hypotension, and chronic or persistent hypotension. The causes of acute hypotension include the following:

1. Traumatic, anaphylactic, or anesthetic shock.
2. Hemorrhage.
3. Acute infectious diseases, including typhoid fever, pneumonia, influenza, diphtheria, scarlet fever, cholera, malaria, typhus fever, etc.
4. Action of tissue extracts (histamine), and drugs (nitrites, etc.).

Chronic or persistent hypotension may result from:

1. Chronic diseases, especially tuberculosis, syphilis, bronchial asthma, chronic arthritis, diabetes mellitus, anemia, status lymphaticus.
2. Focal infections (teeth, tonsils, gallbladder, prostate).
3. Endocrine disorders (myxedema, infantilism, Fröhlich's syndrome, Addison's disease, etc.).
4. Diseases of the circulatory system, particularly where there is severe myocardial degeneration and in acute cardiac infarction.
5. Nervous or physical exhaustion.
6. Essential hypotension.

Aside from cases in which the cause of the hypotension is more or less obvious, there exists also a group of cases in which the low blood pressure is the only apparent finding. Patients in this group present symptoms (easy fatigue, dizziness, etc.) which seem directly attributable to the hypotension, but there appears to be no cause to which the latter can in turn be attributed. The title "essential hypotension" has been given to these cases. It is quite likely that many cases so designated might upon more complete investigation be found to have some obscure cause. There is no doubt, however, that in certain instances there is no discoverable cause of the hypotension, and that the term "essential hypotension" is valid in these.

Friedlander declares that physical examination in such cases shows no organic lesion. The subjects complain of headache, vertigo, and palpitation after moderate exercise. There is marked mental and physical fatigability. The patients lack stamina, have cold, clammy extremities, and are unable to perform the daily routine of their lives. The appetite is capricious, and various dyspeptic symptoms are common. Constipation is found in some, but by no means in all cases. As a rule, the patients are neither neurasthenic nor psychasthenic, and the cases cannot be classified under the psychoneuroses. The condition is most commonly encountered between the ages of 20 and 40.

Lawrence has reported a series of 20 cases of essential hypotension. All of the patients were between 15 and 35 years of age. Only 1 was under 20. There were 14 females and 6 males.

Physical examination was negative except for marked hypotension in each instance. There was no anemia, and no evidence of focal infection. Sleep was poor. While markedly fatigued on arising, the patients generally improved toward the afternoon of each day, and usually felt best after meals, at which time the pressure was also highest. Lawrence emphasizes the fact that the condition is probably often erroneously classified as neurasthenia.

Roberts found that the condition rarely occurs after the age of 40, and that women are affected much oftener than men. According to him, the symptoms in order of frequency are exhaustion, nervousness, headaches, pains in the chest, abdomen, or extremities, indigestion, constipation, backache, dyspnea, insomnia, and palpitation. The 3 chief complaints are exhaustion, lack of endurance, and headache. Hypotension is constant. The patients are not neurasthenic. Apart from visceroptosis or mild focal infections, hypochlorhydria or secondary anemia, no actual pathological condition can be demonstrated.

In the following cases from my practice there is no clear cause for the hypotension, and for some of these it is believed that a diagnosis of essential hypotension is warranted:

Case 1: W. C. T., a male, aged 47 years, complained of dizziness, fatigue, insomnia, chronic constipation, and a feeling of fulness in the upper abdomen after meals. Past history: Gonorrhea at 20; operation for gastric ulcer about 10 years ago, since which time his present complaints have been more or less constant. The patient entered Johns Hopkins Hospital several years ago for diagnostic study, but no organic basis for his complaints could be found. Later he was treated by a gastro-enterologist for colitis, with no relief of symptoms. Wassermann tests on blood and spinal fluid were repeatedly negative. Urinalysis was negative. A recent roentgen-ray examination of his teeth had also proved negative.

Physical examination was essentially negative, except for the presence of some gas in the upper abdomen, and a blood pressure of 100/60.

Treatment with alkalies and sedatives afforded some relief from the digestive symptoms, but the blood pressure fell to 90/40. During the next several months various tonics were administered (iron, arsenic, glycerophosphates, strychnine, vitamin B), with an increase in weight of 5 pounds and some subjective improvement. However, the blood pressure never exceeded 106/60, and when last taken was 80/40, or just 20 points lower than before treatment.

Case 2: E. M. N., a male, aged 48 years, suffered from dizziness, anorexia, tingling sensation in his legs, upper abdominal pains, and belching after meals. An appendectomy had been done some years previously, and most of his teeth had been extracted. A dental x-ray showed the remaining teeth in healthy condition. Urinalysis was negative.

Physical examination was primarily negative, save for a blood pressure of 86/40. The possibility of chronic cholecystitis was considered, but the patient refused a roentgen-ray study because of the expense.

Symptomatic treatment was instituted, and tonics were administered in an effort to raise the blood pressure. The latter varied from 80/44 to 104/60, and when last taken was 96/46, after which the patient failed to return for further treatment.

Case 3: M. N., a female, single, aged 23 years, highly nervous, stated that she had had a "nervous breakdown" 2 years previously, and had suffered since from intermittent weakness and dizziness. The menses had been regular prior to the "nervous breakdown," but since then her periods had been as much as 3 weeks late.

There was no history of serious illness. A tonsillectomy had been done 3 years previously. There was no evidence of focal infection. During the 2 years following the onset of her symptoms, the patient had drifted from one doctor to another, and had been given at least 20 iron injections, also suprarenal tablets, protonuclein tablets, various sedatives and tonics.

Inasmuch as the menstrual irregularity and the other symptoms had begun simultaneously, it was believed that the disturbances might be due to ovarian dysfunction, and a series of injections of corpus luteum extract was instituted. After 4 of these injections there was no change either in the blood pressure or the general condition, and the patient discontinued treatment.

Case 4: K. A. F., a female, married, aged 23 years, on routine physical examination presented a blood pressure of 72/34. At this time the hypotension caused no symptoms, there were no other abnormal findings, and the patient appeared in excellent health. The basal metabolic rate was minus 10 per cent, urinalysis was negative, and the hemoglobin was 90 per cent.

Although there was no evidence of anemia, a tonic of iron and arsenic was prescribed in order to observe what effect, if any, it might have on the blood pressure. After about 6 weeks on the tonic, the blood pressure was taken again, and was found to be 74/34.

During the past 2 years a checkup has been made on this patient's blood pressure from time to time, and it has never been found to exceed 80/40.

About 2 months ago, she began to complain of slight dizziness and easy fatigue; tonic medication was started, and the symptoms promptly subsided, although the blood pressure at the present time is still only 76/38.

Because of lack of coöperation on the part of the patient, or for some other reason, the following cases are not as complete as might be desired. Some of them are cases referred to me by another physician. In these instances only a single call was made, and no opportunity was afforded to observe the progress of the case. These are included to round out the series, and because it is believed that they contain certain points of interest. The first 5, presented very briefly, are cases in which hypotension was associated with menstrual disorders, and was possibly the result of ovarian dysfunction.

Case 5: Mrs. R., aged 43 years, was seen just after her menstrual period, at which time her blood pressure was 84/50. Her chief complaints were dizziness, weakness, and nervousness. She stated that her periods had always been irregular, with scant flow, and were often followed by dizziness.

Case 6: Mrs. J., aged 45 years, complained of fatigue and frequent severe headaches, with nausea and nervousness. These symptoms had existed for 4 or 5 months, and were much worse during each menstrual period. Menses were regular and unaccompanied by dysmenorrhea. Her blood pressure was 80/60.

Case 7: Mrs. H., aged 38 years, complained of dizziness, nervousness, weakness, and numbness of the extremities. She had had these symptoms for 2 months. Her menstrual periods had always been regular, with the exception of the last one, which was 14 days late. Her blood pressure was 102/60.

Case 8: Mrs. B., aged 40 years, complained of dizziness, numbness of the extremities, and palpitation. She was due to menstruate in 6 days, and stated that she always felt weak and tired for 1 week before each menstrual period. She had been treated for low blood pressure for years, and when seen by me her blood pressure was 90/40. She had had an appendectomy, a cholecystectomy, and a tonsillectomy, and there was no evidence of focal infection.

Case 9: Miss S., aged 20 years, had had frequent fainting spells for several years. She was extremely nervous. She suffered with severe dysmenorrhea every month, and she stated that her nervousness was always greatly increased during her menstrual periods. Her blood pressure was found to be 86/50. She had been for several years under a physician's care for the hypotension and nervous symptoms, and during that time her blood pressure had never exceeded 100.

Case 10: Mr. K., single, aged 25 years, at consultation complained of a constant heavy, bloated sensation throughout the abdomen of 2 months' duration, more pronounced on the left side, and somewhat worse after meals, with considerable belching at times. He had been to several doctors, one of whom made a diagnosis of chronic appendicitis from the above symptoms, without examining the patient, and advised operation, which was refused.

Physical examination was essentially negative, except for slight tenderness in the left upper quadrant, and a blood pressure of 90/50.

Questioning revealed that the patient had been partaking of an improperly balanced diet containing an excessive amount of gas-forming foods. He was of a nervous temperament, and it was believed that his digestive symptoms were of a purely functional nature. He was given a preparation of kaolin and mild sedatives, and was placed on a bland diet. He was observed for a period of 1 month, at the end of which there was definite improvement of the digestive symptoms. However, the blood pressure had fallen to 80/40. The patient was discharged at this time, and was instructed to return if his symptoms reappeared.

Case 11: Mr. W., married, aged 40 years, stated that his only complaint was extreme dizziness of 3 days' duration, and of such severity that he was unable to walk without assistance. Contrary to the usual rule, the dizziness was increased on lying down. Three months previously there had been a similar attack, which had come on very suddenly while the patient was walking along the street and had lasted several hours. He was of a neurotic type and seemed to over-emphasize his symptoms.

For years the patient had eaten no breakfast, and frequently no lunch, but ate a very large meal in the evening, and again at bedtime. He declared that he became nauseated if he attempted to take food in the morning. He smoked 30 or more cigarettes and drank 4 cups of coffee daily, but no alcohol.

Physical examination revealed nothing to account for the dizziness, except a blood pressure of 84/50. The patient was quite uncoöperative and refused further examination and treatment.

Case 12: Mrs. C., aged 50 years, and highly neurotic, submitted a typewritten list of her symptoms, consisting of nervousness, insomnia, fatigue, and paresthesia of the neck and thighs, described by the patient as "a distracting pulling or drawing sensation." These complaints were of about 10 years' duration. During that period repeated examinations by various physicians of this city, as well as a thorough diagnostic study in Henry Ford Hospital, failed to reveal any sign of organic disease.

The patient's blood pressure was 96/54. Otherwise a careful physical examination was entirely negative. A hemogram showed no abnormal findings.

Two prescriptions of a sedative nature were given. The patient returned 4 days later, at which time she had not had one of the prescriptions filled, and had taken only 2 or 3 doses of the other, because she thought it was doing her no good. She was advised to take the medicine regularly and to return later, which she failed to do.

In regard to the treatment of hypotension, the measures usually advocated are fairly well summarized by Stevens in the following paragraph:

"The treatment of persistent hypotension varies with the cause. In all cases the patient's habits and method of living must be carefully reviewed. Focal infections, especially, should be sought for and if found removed. In constitutional or essential hypotension a liberal diet of easily digestible food, graduated exercise in the open air, hydrotherapy, and tonic medication are usually efficacious. Nux vomica in full doses is sometimes of value. Digitalis rarely proves beneficial unless there are definite signs of myocardial weakness. Organotherapy is not often of service, although ovarian or corpus luteum extract may sometimes be given with advantage in hypotension developing at the menopause and epinephrine or an extract of the suprarenal gland may occasionally be of benefit when hypotension is accompanied by features suggestive of Addison's disease."

Stevens states that "Timme describes a polyglandular syndrome characterized by intratemporal headache, great fatigability, low blood pressure, low blood-sugar content, abnormalities of skeletal growth and usually sex deficiencies, in which pituitary gland products cause marked improvement."

It has been my experience that the treatment of hypotension is most unsatisfactory. Practically all the measures mentioned by Stevens have been tried. In some instances there has been improvement of subjective symptoms, but in no case has there been any substantial increase of blood pressure.

Preparations of adrenal cortex extract have recently been especially recommended for the treatment of hypotension. This would seem to be a rational procedure, in view of the fact that adrenalectomized animals show changes very similar to the clinical picture in hypotension, including low blood pressure, loss of weight, refusal of food, vomiting, muscular weakness, and lowered metabolic rate (Loeb).

Actually, however, the clinical use of adrenal cortex extract has been disappointing. Loeb states that, except in Addison's disease, extract of the adrenal cortex has no beneficial effect in the various forms of hypotension. Moreover, both Loeb and Rogoff are of the opinion that the use of this extract is not without danger. Rogoff's experimental work on adrenalectomized cats showed that toxic effects are frequently produced by the use of adrenal cortex extract. These toxic manifestations were believed to be due to the presence of histamine in the preparations now available. Rogoff thinks that the clinical inefficacy of these preparations is attributable to traces of histamine, which offsets the beneficial action of the cortical hormone present in the extracts. Loeb ascribes the unsuccessful results to the fact that available commercial preparations may be too dilute or that they deteriorate.

In any event, it appears probable that with the production of more effective preparations of the cortical hormone, the treatment of many cases of hypotension will be more satisfactory than at the present time.

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Liberal Arts Background for Medicine.—Any discussion of the preparation to be desired for admission to a school of medicine should be predicated by an attempt to define the qualities expected in the finished product—the doctor of medicine.

First of all such an individual should have a mastery of the science of medicine and of the application of that science in constructive art.

Secondly such an individual must be a person of culture and refinement commensurate with the highest demands of the society of which he is a part. He must have an education which has prepared him to face the perplexing issues which society presents and to make decisions in accordance with the highest ideals of social welfare. The diagnosis of physical ills often involves an appreciation of social psychology, economics, and governmental procedure. . . .

It is gratifying to note that in 1935 only 11 per cent of the 6,150 entering students had less than 3 years of college residence. Fifty-two per cent had baccalaureate degrees.

This has resulted from one or two causes. Either the shorter period of preparation is inadequate or the undergraduate colleges are persuading students to remain for a longer time in undergraduate courses. . . .

In conclusion: As one engaged in preparing students for medical schools I should like:

1. No reduction of the minimum requirements.
2. Preference in admission given to graduates.
3. Vitalizing and humanizing of college teaching to the end that the term Liberal Arts may have a real meaning.
4. Expansion of medical aptitude tests to include nontechnical cultural background.

Extract from article by RALPH J. GILMORE, Professor of Biology, Colorado College, Colorado Springs, Colorado, *Journal of the Association of American Medical Colleges, May, 1937, p. 157.*

CONSERVATISM IN GYNECOLOGIC SURGERY*

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It is estimated that 1 in every 4 patients seen in the general practice of medicine presents gynecological symptoms.

In treating gynecologic patients it is of extreme importance to learn the essential symptoms for which the patient seeks relief. In pelvic disease these are quite definite and comparatively reliable guides to a correct diagnosis.

Gynecologic surgery is largely elective, and a small percentage of cases only require immediate operation. It is, therefore, the responsibility of the surgeon to see that the patient is physically fit to undergo the necessary surgical procedures with as little hazard as possible. This implies proper preoperative study. The mortality in pelvic surgery is definitely lower than that for other types of abdominal surgery when the usual recognized surgical principles are adhered to. Thus, the same degree of hesitancy may not be shown in pelvic operations that would be expected in undertaking operations in the upper part of the abdomen.

Although the mortality of the operation is small, it is due directly to the operation, and there is some danger in every case. Morbidity and mortality occur in all types of surgery.

We should not overlook the fact that occasionally a patient with everything apparently favorable to a successful outcome will die.

Although the number of mutilating operations done on women is still too great, it is gratifying to note an ever-increasing conservatism. The development of gynecology as a specialty undoubtedly has been the most important factor in this trend.

Conservatism not only infers conservation of structures but preservation of their functions as well. Function is sometimes carelessly destroyed, not that it is necessary, but because it is the easiest way out. This is to be condemned. A conservative operation may be defined as one that saves an organ, or part of an organ that will function, which would otherwise be wholly removed.

Preservation of menstruation and the possibility of pregnancy are important in the life of a young woman. Continuation of menstruation is attained when a functioning portion of the ovary and the uterus, or a part thereof, can be left in place. To make pregnancy possible, there must be a functioning piece of one ovary and a patent portion of a fallopian tube. They may be on the same or on opposite sides.

The tendency to an increasing conservatism in gynecologic practice is evidenced by the more frequent application of orthopedic or nonsurgical principles. Notable among these is the use of the vaginal pessary. Condemned by some, frequently through ignorance, it is an instrument of great value when properly used. Temporarily they are used as a therapeutic test in simple retroversion, and where sterility is a prominent symptom, in the displaced uterus. Pessaries are especially valuable in the treatment of retrodisplacement during early pregnancy and immediately after the puerperium.

Maintaining the fundus in forward position until the fourth month of pregnancy often averts the danger of abortion. And if, after the puerperium, the fundus is found to be retroverted, the use of the pessary will favor involution and frequently prevent permanent displacement and possible subsequent operation.

The pelvic organs, especially the uterus, are frequently blamed for troubles with which they have little or nothing to do. The endometrium is relatively seldom diseased. True endometritis is rare, and leukorrheal discharges are rarely endometrial in origin.

A large percentage of menstrual disturbances are due to endocrine dysfunction. The recognition of these facts has quite well relegated the former "King of Cure-alls," the operation of curettage of the uterine cavity, to the surgical dump heap.

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* Read before the Fifth Annual Postgraduate Clinic of the George Washington University School of Medicine, February 20, 1937.

While the curet is a much abused and at the same time an extremely dangerous instrument, it is an important one. Its use should be largely restricted to diagnosis. It is a necessary aid in the histologic study of the endometrium during the various phases of the menstrual cycle. A diagnostic currettage should always precede radiation of the uterus. If this rule is rigidly adhered to, endometrial carcinoma and uterine polyps will not be missed.

Due consideration must be given to menopausal bleeding, prolonged menstrual function and postmenopausal bleeding, anyone of which may signify malignancy. Our efforts are directed toward early and accurate diagnosis in such cases, and the proper use of the curet is of great help.

Operations for the removal of cystic ovaries are much less frequently seen. We have learned that the so-called cystic disease affecting the ovary is for the most part a physiologic process. In times not so far behind us, reputations were made and incomes increased at the expense of the innocent cystic ovary. Today the ovariotomist is not so popular.

In the treatment of the sterile woman, dilatation and curettage, plastic operations on the cervix, and the introduction of the uterine stem are looked upon as bad practices.

Conservative practice has its greatest application in the treatment of acute pelvic inflammation. The benefits of conservatism here are well known to all. No operation should be performed during the acute stage of the disease, with the exception of drainage of localized abscesses in the pelvis, which can be accomplished with a minimum of difficulty or danger through the vagina. Pelvic structures are most frequently invaded by the gonococcus and next most frequently by the streptococcus. It is important to distinguish between these two, and many lives have been spared by so doing. Immediate surgery was the treatment previously, and the mortality was from 15 to 20 per cent. In more recent times, with the adoption of conservative methods, this has been reduced to about 1 per cent.

Another opportunity to apply conservative methods with good results is with myoma of the uterus in women of the reproductive age. Myomectomy should be given preference when possible.

With increased knowledge, gained from a longer experience in the proper use of radium, a further decrease in the indication for removing the uterus has occurred. In the treatment of hemorrhage of proved benign cause in the woman of middle age, intra-uterine radiation is much more satisfactory from the standpoint of surgical risk and economy than hysterectomy.

Operations, such as high amputation of the cervix, have been discarded to a great extent. Very little importance is attached to lacerations of the cervix per se, but when complicated by infection, must be treated. The electrothermic cautery in the treatment of the infected cervix is preferable to the above-mentioned procedures. The endocervix, with its glandular structure, lends itself as a frequent and important focus of infection. Sturmdorf aptly termed it the "tonsil of the uterus."

Radiation methods have supplanted surgery in the treatment of carcinoma of the cervix. Total hysterectomy for fundal carcinoma is still thought best, unless contraindications exist, although excellent results have been reported in the treatment by radiation.

In the treatment of myoma of the uterus, when hysterectomy is indicated, there is a widely varied opinion among gynecologists, and discussion is continually arising as to whether a total or a subtotal operation should be done. In deciding this question, a great deal depends upon the training and experience of the operator. Also, the condition of the cervix is of prime importance in this decision. If it is badly infected and the physical condition of the patient permits the increased operative risk, it should by all means be removed. Otherwise, a subtotal hysterectomy is performed, with deep cauterization or conization of the cervical canal done as a safeguard. Arguments advanced in favor of a total operation are that carcinoma occurs in the remaining cervical stump subsequently in about 1 per cent of cases, and carcinoma is associated in about 5 per cent of uterine myomata.

Vaginal hysterectomy has as its chief indication prolapse of the uterus. In patients of advanced age who are debilitated, it can be done with the least amount of risk. As compared with a properly executed abdominal hysterectomy in other types of cases it has no advantages.

In the management of gynecologic conditions, age, physical condition, and social and economic status of the patient are influencing factors. Fundamentally, the aim of the gynecologist in his practice should be conservatism.

To repeat, conservatism in gynecology not only implies conservation of the reproductive organs, but preservation of their functions as well.

ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"Irradiation of the Pituitary Gland in Functional Disorders of the Female,"* **J. Kotz, M.D., F.A.C.S.**, and **Elizabeth Parker, M.D.**, George Washington University School of Medicine.

With the rapid strides which have been made during the past decade in the understanding of female endocrinology, a need has arisen for some effective method of treatment of the various functional disorders. This need has been met to a very satisfactory degree in the use of fractional doses of X-ray to the pituitary gland. The use of irradiation for the correction of functional disorders of the female is recent in this country, although it has been used fairly extensively abroad. It was introduced by Haufbauer in 1922 before the German Gynecological Conference. Van de Valden in 1915 recommended small doses of X-ray over the ovaries in the treatment of functional amenorrhea. Since this time there have been an increasing number of reports in the literature on the efficacy of this method of treatment.

In using X-ray to the pituitary gland, no pretense is made in explaining its action. It has been found effective, which must be sufficient for the time being. There is wide divergence of opinion as to its modus operandi. However, the exclusive use of X-ray is not recommended. In cases in which organotherapy is indicated and potent products are available, they should be used. But at the present time physiology and chemistry are not sufficiently developed for organotherapy to be effective when used alone. The identity and individuality of some of the hormones have not been determined, and in many cases it has not been proven which hormones cause certain reactions. Also, endocrine disorders are not the result of the lack of, or over-abundance of a single hormone with complete normalcy of the other glands. The abnormal function of one gland is usually accompanied by decreased function in some of the other glands of the endocrine system with compensatory hyperactivity of others, depending upon the normal interaction of the glands.

Irradiation of the pituitary gland is used effectively in many of the functional disorders of the female because the causes of most of these disorders differ from each other in degree more than in kind, and the degree of the disturbance of the ratio of the female sex hormones is the important factor in determining the clinical manifestations of the disturbance. Also, the pituitary is the master gland of all the endocrines, the ovary being completely under its dominance. Most of the functional disorders of the female are not primary in the ovary but are the result of improper pituitary action.

For irradiation therapy to be effective, the cases must be carefully selected. Thereafter, there are no contraindications for its use, since there are no ontoward side-effects.

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* Presented February 17, 1937.

The Treatment of Pulmonary Abscess; Review of Thirty-One Cases at the Wisconsin General Hospital. Since 1927 there have been 31 cases at the Wisconsin General Hospital in which pulmonary abscess has been the primary diagnosis. Those cases, in which pulmonary abscess was merely an incidental or postmortem diagnosis as part of a terminal septicemia (as in osteomyelitis or pyelonephritis) or as part of what was chiefly a bronchiectasis with multiple moderate sacculations, have been omitted.

General Description. There is little of unusual interest, so far as the general disease picture is concerned, in these thirty-one cases. The diagnosis, as a rule, could be made by the history of the case alone with the story of copious foul sputum associated with a very debilitating febrile course. Physical signs were often not typical of cavitation, and x-ray, in each instance, gave decisive information. . . .

Summary and Conclusions. Thirty-one cases of pulmonary abscess have been described.

The age of the patients in this group bore no remarkable relationship to the mortality.

Almost two thirds of the eight postoperative abscesses were confined to the right lower lobe of the lungs, whereas only one fourth of those abscesses not postoperative in origin were located there.

These were chiefly chronic abscesses. Their average duration before admission was 41 months.

Twenty-three cases were treated by surgery, and 8 were not given surgical treatment.

The mortality in the operative cases was 52 per cent; in the nonoperative cases it was 50 per cent.

All of the surviving surgically treated cases were either well or "clinically cured" on discharge while only 1 case, and that a very acute one, was improved without open drainage. The causes of death in the fatal cases have been detailed.

The operative mortality in 13 cases with single abscesses was 38 per cent; in 10 cases with multiple or multilocular abscesses it was 70 per cent.

The operative mortality in 14 cases of less than 1 year's duration was 28 per cent. In 9 cases of more than 1 year's duration the operative mortality reached 89 per cent.

Although the number of cases reported is small, the striking correlation of a long duration of symptoms and multiplicity of abscesses with a high mortality, make it appear justifiable to conclude that the longer symptoms have been present the more likely are the abscesses to be multiple and both of these factors, separately and together, result in a very great increase in the operative and nonoperative mortality.

Extract from article by Peter A. Midelfart, M.D., and Joseph W. Gale, M.D., Madison, *Wisconsin Medical Journal, May, 1937*, p. 373.

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IMMUNOLOGY

The Practicing Physician's Opportunity

Diphtheria, smallpox, whooping cough measles, scarlet fever, typhoid fever, and tuberculosis are prominent subjects for discussion in modern immunology. Although each disease does not yield to immunological procedures with the same high efficiency attained in diphtheria and smallpox, the physician should be fully cognizant of the possibilities. Especially should the physician in contact with the public in private practice be aware of modern public health measures and the present facilities in the field of prevention of the diseases which are still too prominent in morbidity and mortality in early life and of too serious portent in sequelae occurring in later life. All infants of 6 months to 1 year of age should routinely receive toxoid with view to the creating of an active immunity to diphtheria. Recent observations by Park, and certain Toronto investigators, suggest the necessity of Schick tests for measuring immunity at 6 months, 1 year, and routinely thereafter. There appears to be some evidence in favor of 2 injections rather than 1 of the alum precipitate toxoid. Smallpox vaccination, the efficiency of which is established, had better be instituted at this time.

Sauer's whooping cough vaccine in relatively large dosage may frequently be administered with some hope of profit. In younger infants the dose may be split into multiple smaller injections. The ravages of the disease are greatest in early infancy. Attention need but be called to the high mortality rate in the frequent complication of whooping cough, bronchopneumonia. There is definite assurance no harm can be done in its administration. Absolutely successful results should not be generally predicted, but it may be stated there is offered a chance to a child already suffering from a serious disease or handicapped by a special liability to tuberculosis to escape an added burden.

Measles may be modified greatly in severity by use of the immune convalescent serum, blood or placental extract. Although the latter yields effective results, not infrequently rather severe local reaction follows. With a "measles" year in Washington in the offing it would be most appropriate to establish pools of convalescent serum. Undoubtedly lives may be saved by treating the weakened siblings or other contacts of sufferers from the disease with serum. Indeed, the symptoms are often so mild in those so protected that the disease is hardly recognized. It should be remembered that the use of immune blood or serum creates an evanescent passive immunity, lasting but a few days. The aim should be modification in those exposed, not a general prevention.

Scarlet fever prophylaxis, although never on the plane of diphtheria, offers frequently more to the recipient than generally conceded. Dextrose freely administered, the fasting stomach, injection given at night, seem according to observers, notably in Philadelphia, to prevent severe reactions. Typhoid prophylaxis to those leaving the city at this time of the year for camps in rural communities should be invariably administered.

Finally, the physician should know the technic and apply in practice the intradermal Mantoux tuberculin test. At the time of making routine physical examinations of children this measure should be invariably instituted. A positive reaction followed by chest X-ray is often revealing. The infected adult in the family where the positive child is found must be sought. One should not be forgetful that a servant often furnishes a focus. Before allowed to serve in a family of young children the servant should be Mantoux tested and X-rayed. Uninfected children in the household may be thus protected. The child with the positive skin test may escape a heavier load.

The practice of the simple principles of immunology by general practitioners is a duty, an obligation to the patient and community. It pays dividends in lives saved and satisfaction in the knowing that one has performed faithfully his duty.

To summarize: 1. Diphtheria and smallpox prevention at the age of 1 year. Diphtheria toxoid injection must be followed with at least yearly Schick tests to age of 7 years for purpose of checking immune response.

2. Whooping cough (Sauer's vaccine) when the infant is generally below par with sources of infection present. Parent should be frankly informed of the present status of this type of prophylaxis—vide Sauer's reports also New York Health Department Statistics.

3. Measles prevented or much better modified by immune convalescent serum, parents blood or serum, placental extract. A passive evanescent immunity is thus created. At present the general idea should be to mitigate the symptoms not actually to prevent. Coöperate with the public health authorities in keeping of statistics of numbers treated prophylactically and the results during the coming "measles" year in Washington.

4. Scarlet fever prophylaxis is worthy of trial. Nurses or others with much opportunity of exposure when Schick positive, should be treated. Attention to certain details seem to lessen severity of reaction.

5. Typhoid prophylaxis generally not necessary in infancy, should be given to adults or adolescents when going to places having doubtful water and milk supply.

6. Every physician treating children or the young should be familiar with the Mantoux test, using it with the routine physical examination. The disclosing and subsequent eliminating of sources of tuberculous infection in a household is of prime importance as a public health measure.

STATISTICAL REPORT OF THE CENTRAL ADMITTING BUREAU FOR HOSPITALS

FIRST QUARTER OF 1937

Foreword

No attempt has been made to stress any particular set of figures, nor are any of them to be construed as being important if perchance a little extra emphasis has been put upon them. Rather they should be looked upon as presenting a true picture of the work done by the Central Admitting Bureau for Hospitals and the hospitals themselves on cases sent to them through the Central Admitting Bureau for Hospitals in their relentless war on illness.

The report is by no means complete, chiefly because of the limited time and personnel available to collect, tabulate and analyze the material.

An effort has been made to collect all information that would seem to be directly the result of the operation of the organization and the hospitals coöperating with it.

This report is therefore offered with the knowledge that it is definitely limited in scope but with the firm belief that it is and will be of great value to those interested in the Central Admitting Bureau for Hospitals and the work done in the hospitals through the Central Admitting Bureau for Hospitals.

Owing to limitation of space the editors of the Annals have had to eliminate much of the interesting data included in this report. The report has been prepared by Mr. Ross Garrett, Executive Director of the Central Admitting Bureau for Hospitals, and his Staff.

Clinic Passes

During the first 3 months of 1937 there were 8,581 clinic passes issued to ambulatory patients. These passes had a "time value" of 2,890 years, i.e., 1 patient could visit 1 clinic per day every day for 2,890 years.

The approximate value of the passes issued was $528,000.00 if their "full visit possibilities" were utilized.

	Per cent
Passes issued for 90-day periods or more	81.0
Passes issued to people who agreed to pay something for each visit	27.1
(Of these 12.2 per cent agreed to pay the full rate of $0.50 per visit, and 14.9 per cent agreed to pay part of the established rate.)	

	Per cent
Passes issued to people who were unable to pay anything	72.9
Applicants for clinic treatment rejected for various reasons	1.6
Applicants employed on Works Progress Administration projects	9.4
Applicants listed with the Public Assistance Division	5.7

There were 3,583 extensions in time on already existing clinic passes.

	Children's Hospital	Columbia Hospital	Emergency Hospital	Episcopal Eye, Ear, & Throat Hospital	Garfield Memorial Hospital	Georgetown University Hospital	George Washington University Hospital	Providence Hospital	Total
30-day	66	3	64	29	87	41	17	56	363
60-day	280	19	96	330	127	140	94	185	1271
90-day	811	123	345	490	528	352	230	358	3237
Over 90 days	746	396	492	375	560	463	250	428	3710
Total	1903	541	997	1224	1302	996	591	1027	8581
Extensions	938	165	461	468	543	464	177	367	3583
Part-pay	344	284	83	124	180	104	55	107	1281
Full-pay	202	113	116	55	214	121	127	99	1047
W.P.A.	212	14	68	138	98	113	35	128	806
P.A.D.	83	4	119	81	69	54	29	52	491
Free passes	1357	144	798	1045	908	771	409	821	6253
Rejections	28	3	10	26	25	22	12	8	134

From the above tabulation it is apparent that although more passes are issued to the clinic in Children's Hospital, with Garfield Memorial and Episcopal Eye, Ear and Throat Hospitals ranking second and third, respectively, the relation of patients able to pay part of their bill is not in the same order. The patients accorded facilities in Garfield Memorial Hospital in relation to the total number given passes to Garfield Memorial Hospital's clinics had paying possibilities 1 per cent greater than those attending Children's Hospital clinics, whereas those going to Episcopal Eye, Ear and Throat Hospital ran a very poor third.

Bed-patient Analysis

Five thousand three hundred and eighty-nine (5,389) people applied for hospitalization during the first quarter of 1937, of which 64.9 per cent were people who had previously received treatment through Central Admitting Bureau for Hospitals facilities; 35.1 per cent were cases never before registered at the Bureau.

Type of Cases Handled

New Cases	*Old Cases*	*Total Cases Handled*
1,889	3,500	5,389

Arrangements for hospitalization were made for 35.7 per cent of the applicants and 19.4 per cent received extensions of time on already existing arrangements; 5.4 per cent of the cases applying were rejected for admission. These cases were referred to the Board of Public Welfare, Medical-Dental Service Bureau or to private physicians. Service and consultation facilities were accorded to 21.7 per cent of the applicants, and it was found necessary to transfer 0.5 per cent to some other institution.

Disposition of Cases Handled

Admitted	1,542
Re-admitted	384
Extensions	1,047
Rejected	290
Service	1,168
Pending	930
Transferred	28
Total Cases Handled	5,389

Of the patients admitted and re-admitted to the Chest hospitals through the Central Admitting Bureau for Hospitals facilities 66.3 per cent were given care in 4 hospitals—Columbia; Episcopal, Eye, Ear and Throat; Garfield Memorial; and Providence. The remainder of the cases were fairly evenly distributed between the other hospitals with the exception of Homeopathic Hospital which received only 0.6 per cent of the cases.

Distribution of Cases to the Chest Hospitals

Children's	167
Columbia	330
Emergency	186
Episcopal, Eye, Ear and Throat	311
Garfield Memorial	303
Georgetown University	176
George Washington University	110
Homeopathic	11
Providence	332

TRANSACTIONS OF THE SOCIETY

Stated Meeting, May 12 and 19

(*Continued from May issue*)

Reports of Committees

Committee on Public Health

SUBCOMMITTEE ON TUBERCULOSIS

Recommendations contained in the report of the Subcommittee on Tuberculosis, presented before the Society, March 3, 1937*:

An adequate program for the control of tuberculosis in the District of Columbia should be adopted, as follows:

I. The medical profession should coöperate with the health authorities by observing regulations prescribed by law for the control of tuberculosis.

II. Existing facilities should be reorganized and utilized as follows:

A. The Health Department's Tuberculosis Clinic should have the following functions:

1. To act as a diagnostic center for indigent patients.

2. To recommend admission to the city's tuberculosis hospitals through the Permit Bureau of the Board of Public Welfare.

3. To act as a repository for records of all cases of tuberculosis.

4. To supply adequate nursing follow-up of active cases and contacts.

5. To promulgate continuous publicity and educational program to make the general public cognizant of the danger of tuberculosis.

6. To provide further observation and supervision of all indigent cases of tuberculosis discharged from the city hospitals.

B. That in regard to the Adult and Children's Tuberculosis Sanatoria the following should be done:

1. Merge the Adult and Children's Tuberculosis Sanatoria.

2. Divorce the medical direction of the Sanatorium from the business management.

3. Provide a full-time Medical Director without outside practice.

4. Reserve the sanatorium beds at Glenn Dale for those patients offering the best hope for rehabilitation.

5. Modernize sanatorium treatment at Glenn Dale in every respect.

6. Make the size of the staff at Glenn Dale conform at least with the minimum requirement as outlined by the American Sanatorium Association.

C. That in regard to the Gallinger Municipal Hospital the following be done:

1. Limit the tuberculosis facilities to the following groups:

(a) Those patients offering little hope of rehabilitation.

(b) Patients requiring diagnostic study which is not feasible at the Tuberculosis Clinic.

(c) Temporarily hospitalize patients pending vacancies at the Glenn Dale Sanatoria.

2. Urge the profession generally, the Medical Schools of the District of Columbia, and the nurses' training schools to make use of the facilities at Gallinger Municipal Hospital for teaching tuberculosis.

3. Urge, because of the inadequacy of the existing physical plant for the care of the tuberculous at Gallinger Municipal Hospital, that a building to house at least 300 patients be erected at this institution.

III. That the following general recommendations be adopted:

1. That a single department of thoracic surgery be developed for all city hospitals dealing with tuberculosis.

2. That adequate facilities be provided for the domiciliary care and isolation of old chronic open cases of tuberculosis who do not require hospital care and for whom no satisfactory curative treatment has as yet been devised.

3. That an advisory board of physicians who by training and experience have special knowledge of problems of tuberculosis control be formed to assist the public officers charged with the control of tuberculosis in the District of Columbia. (In addition to its other duties this board should regularly inspect all public institutions dealing with tuberculosis in the District of Columbia and recommend to the proper authorities such improvements as it deems desirable.)

4. That the Health Department Tuberculosis Bureau's Director be a full-time officer available for consultation in indigent cases.

The following resolutions were adopted:

1.† Whereas, The Medical Society of the District of Columbia has expressed its approval of the recommendations contained in the report of the Subcommittee on Tuberculosis of the Committee on Public Health, presented before the Society on March 3, 1937; and

Whereas, It is believed that a better utilization of the existing facilities for the control of tuberculosis in the District of Columbia may be had if these recommendations are put into effect; be it

Resolved, That the Secretary of the Medical Society of the District of Columbia be instructed to send copies of these recommendations to the Director of the Department of Public Welfare and the Health Officer of the District of Columbia.

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* Adopted by the Society, May 12, 1937.

†Adopted by the Society, May 12, 1937.

2.* WHEREAS, The number of hospital beds that will be available for the care and treatment of tuberculous patients in the District of Columbia will be grossly inadequate even after the opening of the new sanatorium that is being erected at Glenn Dale; and

WHEREAS, The facilities for this purpose at the Gallinger Municipal Hospital, where approximately one fourth of the available beds will be located, are inadequate both as to the physical plant and personnel; and

WHEREAS, Because of the remoteness of the Glenn Dale institution and its inaccessibility, it will be necessary to have in the city an institution to serve as a clearing house for tuberculous patients in order that the most efficient use of the institutions for care of these patients may be had; and

WHEREAS, In the interest of economy and efficiency of operation the logical place for such an institution is on the site of the Gallinger Municipal Hospital; therefore, be it

Resolved, That it is the opinion of the Medical Society of the District of Columbia that efforts should be made to obtain from Congress an appropriation for the erection and equipping of a building to house at least 300 patients at the Gallinger Municipal Hospital to replace the present makeshift facilities of the Tuberculosis Division of this hospital; and be it further

Resolved, That the coöperation of the District of Columbia Tuberculosis Association, the Federation of Citizens' Associations, other civic organizations, and the Press be sought to the end that the required appropriation may be obtained.

SUBCOMMITTEE ON COMMUNICABLE DISEASES

The Subcommittee on Communicable Diseases submits herewith the following report:

Among the accomplishments of your subcommittee was the preparation of a circular regarding diphtheria immunization, which was sent to all of the members of the Medical Society of the District of Columbia, urging their coöperation and active participation in the program of the Department of Health of the District of Columbia in securing wide-spread immunization of preschool and school children. The subcommittee met with the Fellows of the American Academy of Pediatrics resident in the District of Columbia and with some of the full-time physicians in the Bureau of Child Hygiene of the local Department of Health and of the Children's Bureau of the United States Department of Labor. At these joint meetings those present exchanged ideas freely and adopted practicable means for bringing about wide-spread diphtheria immunization in the community. Through the efforts of your subcommittee the Health Department offered to supply material for Schick testing and toxoid for immunizing injections to every licensed physician in the District of Columbia who applied for them.

On the post-cards and other notices of the weekly meetings of the Medical Society of the District of Columbia, slogans keeping the matter of immunization against diphtheria constantly before the membership were prepared each week by your subcommittee.

An editorial, giving figures which showed the District of Columbia to be about where it was 10 years ago in diphtheria morbidity and mortality and, therefore, showing that as a community we were very much behind more progressive municipalities and states in the matter of public health, was prepared by the Chairman of your subcommittee and published in the November number of the Medical Annals of the District of Columbia.

The Committee on Public Information was supplied by your subcommittee with material for use over the radio or in the press, brief statements with regard to the prevention of communicable diseases, including articles prepared upon the subjects of diphtheria immunizations, whooping cough prevention, typhoid fever, general measures to be used in the control of the spread of all contagious diseases, and also upon diarrhea and dysentery. Your subcommittee was preparing publicity material for a number of other diseases but the response of newspapers to publication of this material was so poor that the Chairman of the Committee on Public Information notified us by letter that it was scarcely worth while to continue the preparation of these articles.

Our recommendations for future plans by the Medical Society of the District of Columbia are already revealed in the activities enumerated above for the reduction in morbidity from communicable diseases. It is our unanimous opinion that summer and early fall are the seasons of the year when the practice of active immunizing injections should be carried out. In fact, they may be started the latter part of April or early in May. Every member of this Society should have, easily within reach, materials to do Schick tests and diphtheria preventive inoculations. If he is a specialist and does not care to do this work himself, he should constantly keep before the families containing preschool children the enormous value of diphtheria prevention and how easily it is accomplished. Specialists who do not do this type of inoculations can do much in the way of education and can refer the child back to the family physician for this purpose.

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* Adopted by the Society, May 19, 1937.

We believe that the Health Department should lead in these intensive campaigns of health protection, not only for diphtheria but in the many diseases which may be brought under control. We are perfectly sure that the actual work of immunizing should be done by physicians, members of this Society, who are responsible for the care of preschool children. Other communities have accomplished this through the practicing physicians with the members of the health department doing a minimum of it.

Thirty-five or 40 per cent of the practice of children's specialists consists in preventive pediatrics. This is based on a statement made by the Secretary of the American Academy of Pediatrics. Every practicing physician is likewise engaged in disease prevention but the family physician in the District of Columbia is not doing enough of preventive pediatrics. This is evidenced by the figures quoted in the editorial above mentioned, showing that there has been no reduction in diphtheria morbidity and mortality in the District of Columbia in the past 10 years, which greatly contrasts with the conditions in more progressive and active communities and states. It will be a pleasant and gratifying surprise to see what can be accomplished when members of the Society are roused to the needs of the situation and really put their shoulders to the wheel.

H. H. DONNALLY, *Chairman*
EDGAR P. COPELAND
J. H. MCLEOD
WILLIAM S. ANDERSON
M. H. GROSVENOR
Subcommittee on Communicable Diseases.

SUBCOMMITTEE ON MATERNAL WELFARE

In the 2 years of its existence the subcommittee has been concerned chiefly with the object of setting up a maternal mortality survey on a current basis.

Much has been said and written about the unfavorable position of the United States in the family of nations in respect to its higher maternal mortality, and further uncomplimentary things have been said about the District of Columbia in its relationship to other jurisdictions within the United States. Investigation into the reports on this matter show that there has been very little effort to break down the figures into the actual causes of death in these cases. Deaths have been reported as maternal which were in fact not so and deaths have been reported due to other causes which were in fact related with obstetrical events. The Medical Society of the District of Columbia and the Washington Gynecological Society in establishing this joint committee desired to find out exactly what is the situation in Washington and where efforts should best be directed to improve it if the findings are not good.

The current survey which is about to be inaugurated will involve a careful detailed study of each maternal death as it takes place in the District of Columbia during the next 1 or 2 years. The resources of the 2 societies mentioned and also those of the Children's Bureau of the United States Department of Labor, and of the Bureau of Maternal and Child Welfare of the local Department of Health have all been joined to make this survey possible.

Reference is made to previous reports made by this committee on May 20, October 7, 1936, and April 7, 1937.

On October 7, 1936, the Society passed a resolution pledging its coöperation and its assistance in the survey. On April 7, of this year, the Society elected an Obstetrical Board to carry out this survey and to study these deaths as they may occur. The Board, which was then elected, consists of Drs. Herbert P. Ramsey, Chairman; J. J. Mundell, William J. Stanton, E. W. Titus, and Prentiss Willson.

At the last meeting of this subcommittee the business of carrying forward this survey has been turned over to this Board which the Society elected to serve until the survey be completed.

Between 60 and 80 maternal deaths occur here in every year and we have from 8,000 to 10,000 live births annually in this district. The full coöperation which the Society pledged last October will now have an opportunity to be manifested. The subcommittee appeals to other members of the Society who have anything to do with delivering babies, to make a special effort from this time forth to see that his office records and his hospital records in respect to his obstetrical care are complete and detailed. There will be also absolute need for the same accuracy in the keeping of dispensary records on antenatal and postnatal patients. Members of the Subcommittee on Maternal Welfare, having turned this survey itself over to its elected Board, will now proceed to contact the Obstetrical Departments of all hospitals to ask their full coöperation in the matter of keeping of accurate records on all obstetrical patients, private and ward, and the accurate keeping of dispensary records. This applies not only to history and examination and notes concerning the course of labor and manner of interference if any, but also in fatal cases it will involve a determined effort on the part of the practitioner to get if at all possible a postmortem examination of the deceased. Only in this accurate scientific way can we arrive at a detailed exact knowledge of the cause of death and all of the factors, medical, economic, hospital and otherwise that enter into the death of the patient.

At the conclusion of the survey the findings will be brought to the societies for consideration. Since the Board will assume the survey from now on the subcommittee will address itself to the many other matters in regard to improvement of maternal, antenatal and postnatal care in the District of Columbia, both private and ward. Is it too much to ask that each member of the Society lend his whole-hearted coöperation to all the implications of this survey which will be conducted and reported with absolute honesty?

Herbert P. Ramsey, *Chairman*
W. Preston Haynes
Alec A. Preece
Howard F. Kane
Radford Brown
J. Bay Jacobs
Subcommittee on Maternal Welfare.

ACTIVITIES OF SECTIONS

The Section on Neurology and Psychiatry organizes for the coming year:

John P. H. Murphy, *Chairman*
Joseph L. Gilbert, *Vice Chairman*
James W. Watts, *Secretary-Treasurer*
Walter Freeman
Herbert H. Schoenfeld } *Executive Committee*
Roger S. Cohen

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS

The regular meeting of the Washington Society of Pathologists, Inc., was called to order at 1:30 P.M., May 1, 1937, in the Army Medical Museum by the President, Dr. R. M. Choisser. The minutes of the previous meeting were read by the Secretary, Captain Elbert DeCoursey, and approved.

The Society accepted the nominations of the Council, and the following were elected officers for 1937–1938: Oscar B. Hunter, President; J. W. Miller, Vice President; Elbert DeCoursey, Secretary-Treasurer; Eugene R. Whitmore, for 2-year Councilor; R. M. Choisser for 1-year Councilor.

It was voted that the annual dinner in honor of Dr. Harold V. Connerty, who has taken a post away from the city, should be held on the last Saturday in May (May 29) at 7 P.M., at the Cosmos Club.

Presentation of Cases

Dr. L. C. Milstead presented the case of a single girl, aged 22 years, who had a large solid, soft tumor of left ovary, the size of a large cantaloup and containing areas of hemorrhagic necrosis. The patient was first admitted to the hospital in December, 1936, complaining of persistent cough, progressive loss of weight and strength, difficulty in breathing and "asthmatic" attacks, all of about 2 years' duration but becoming progressively severe. Physical findings included brassy cough, hoarseness, bilateral parasternal dulness, tachycardia, symmetrical sibilant râles. X-ray film revealed the presence of very large opacities in the hilar regions of both lungs, filling the mediastinum and involving the medial lung fields bilaterally. The presumptive diagnosis was lymphosarcoma. Deep x-ray therapy, 400 K.V. light doses, by the fractional method, was employed. The lesions melted rapidly. About March 15 she had her menstrual period at usual time, but more profuse and painful than usual. A rapidly developing sense of weight and fulness and a mass in lower abdomen followed. Sections disclosed anaplastic epithelial tumor composed of moderate-sized round epithelial cells with vesicular cytoplasm and pale nuclei containing large nucleoli. The cells formed large, irregular nests and were supported by a delicate stroma containing round cells. "I am wondering if this is not a malignant sex-cell carcinoma."

In the discussion, dysgerminoma, lutein-cell tumor and small-cell adenocarcinoma of the ovary were considered.

Dr. Harry A. Davis presented the case of a white woman, aged 52 years, who was admitted to Columbia Hospital for Women in October, 1936, complaining of vaginal bleeding. Curettment of the uterus was preformed and the patient remained well until March, 1937. She was admitted to George Washington University Hospital on April 1 complaining of hematuria. A soft fluctuating mass was felt in the right adnexal region and the cervix uteri appeared to be eroded. A diagnosis of carcinoma of the cervix with extension to right adnexal region was made. While a biopsy from the cervix uteri was being obtained under nitrous-oxide anesthesia, the patient suddenly collapsed and died upon the operating table. Necropsy revealed the peritoneal cavity to be filled with fresh blood (approximately 2,000 cc.). The right broad ligament was thickened, and in its upper portion close to the right fallopian tube there was a small opening measuring 2 mm. in diameter through which fresh blood was oozing. Between the layers of the ligament there was a large multiloculated cavity containing recent and old blood clot. Several small vesicles containing clear fluid were present in the clot, but there was no evidence of a fetus. The lower portion of the right ureter was involved in the mass. The uterus was somewhat enlarged, the endometrium being absent as a result of the recent curettment. No gross evidences of neoplasm were present in uterus or cervix. The right fallopian tube was thickened, and in its mid-portion the lumen was continuous with the hemorrhagic area in the right broad ligament. The remainder of the adnexae appeared to be normal except for small cystadenomata in the ovaries. No evidences of metastases were present in the liver, lymph nodes or other abdominal viscera. Examination of the right lung showed the presence of three small hemorrhagic infarcts in the lower lobe, and in the inferior branch of the right pulmonary artery a small, clear vesicle was present. An anatomic diagnosis of ectopic hydatidiform mole associated with chorioepitheliomatous degeneration was made. Microscopic studies confirmed this diagnosis.

In the discussion the diagnosis of chorioepithelioma was agreed upon.

Dr. Walter Freeman presented the case of a man about 50 or 55 years of age who complained of pain down the right arm. The x-ray film showed a fairly large mass of the pulmonary apex, which progressively increased in size in November and in December. Pain in the chest radiated down the arm. There was anesthesia and disturbance in the sweat secretions which indicated involvement of the sympathetic nerves. Horner's syndrome was present. Chordotomy of the third cervical segment on the left was done. The same evening the patient appeared to be entirely comfortable but later developed cachexia and died. At autopsy the right lung, thoracic cage and a large tumor mass which had eroded through the ribs, the vertebral column, and into the vertebral canal (on the outer aspect of the dura), were found. In the left suprarenal there was a large rounded mass which practically destroyed the whole gland. The brain showed a mass about 5 cm. in diameter in the left occipital pole. The sections showed a very wildly proliferating type of growth with enormous giant cells, and the question arose whether this was a primary malignant lung neoplasm or whether it represented the so-called Pancoast tumor or superior pulmonary sulcus tumor.

In the discussion it was said that: Pancoast considered the superior sulcus tumor to be derived probably from the fifth branchial cleft; Connally of England and the Mt. Sinai (New York City) group think that the tumor is probably a terminal bronchiolar carcinoma that just happened to be in the superior pulmonary sulcus; Kelman thinks that the carcinoma comes from an unknown epithelial element in the seventh cervical paravertebral region; Frost has found a sulcus tumor of this region which he has called a sympathoblastoma; Lereboullet reported a combination lung carcinoma and tuberculosis extending from the apex to give this syndrome.

Dr. Robert J. Jermstad presented the case of a white man, aged 43 years, whose symptoms began 8 months ago with headaches and pains in shoulders and joints. An x-ray examination revealed numerous areas of osteoporosis and bone absorption. The skull had a rat-eaten appearance and numerous areas were noted in the ribs and pelvis. The blood calcium was 14 mg. per 100 cc. of blood and in view of this and the x-ray findings a diagnosis of osteitis fibrosa cystica was made. The parathyroids were subjected to x-ray treatment with disappearance of the pain in the shoulders. A few days ago a biopsy was done with removal of a portion of an affected rib. Examination of this specimen revealed a typical multiple myeloma of the plasma-cell type. The patient is at present free from pain.

Dr. W. P. Argy reported the case of a woman, aged 70 years, who was first seen in June, 1934, complaining of stiffness and pain in the feet following a fall. She tired easily, was losing weight, and had glycosuria and anemia. Physical examination revealed a fairly well advanced arteriosclerosis with arteriosclerotic heart disease, a few shotty glands in the anterior triangle of the neck, and a mass of fairly large discrete freely movable glands in the left axilla. The reflexes in the lower extremities were equally exaggerated and there was some diminution in vibratory sensation. It was concluded that she had a microcytic, hypochromic anemia, arteriosclerosis and mild diabetes. The disturbance in the legs was attributed to the injury sustained and the deformity of the back. The axillary glands were removed under gas-ether anesthesia, and since varied reports were obtained from local pathologists the tissues were placed on the lymphatic tumor registry and the consensus of opinion was Hodgkin's disease and tuberculosis. She was last seen in March, 1937, and at that time was in excellent health with no evidence of any glandular enlargement.

Dr. C. H. Binford presented the case of a white man, aged 61 years, a cook, who came into the United States Marine Hospital complaining of 10 days' pain in the left side of the abdomen, initiated by chills. X-ray study of the gastro-intestinal and genito-urinary tract and chest were reported negative. Exploratory laparotomy was done which revealed a nodular mass, 5 by 7 inches which involved the retroperitoneal glands in the left hypochondrium. The small intestine and stomach were adherent to the mass. The spleen and left kidney were normal. A biopsy taken for examination. The blood picture normal. The Kline test was negative. The A-Z test was positive. The diagnosis was embryonal carcinoma.

Dr. Roger M. Choisser presented the case of a white woman, aged 34 years, a clerk, whose symptoms began 6 weeks before with headache. This became progressively worse requiring Veronal for relief. She entered the hospital in coma. The pupils were irregular, the reflexes hyperactive, the Babinski positive, the neck rigid and the spinal fluid turbid with many red blood cells. There was complete relief of symptoms for a few hours after a spinal tap, but she lapsed into coma and died 4 hours later. Autopsy revealed hemorrhagic neoplastic nodule at the base of the left lung and multiple soft hemorrhagic intracerebral lesions. The color and consistency of the lesions were like that of thick chocolate pudding. Microscopic examination showed malignant melanoma. Subsequent history revealed that a pigmented mole had been removed from the left side of the neck by fulguration 6 months previously. There had been no local recurrence.

In the discussion the advisability of fulguration of skin moles was questioned.

The meeting adjourned at 3:45 P.M.

NEWS AND PERSONALS

Dr. Leland Ossian Howard, who was unanimously admitted to Honorary Membership in the Medical Society of the District of Columbia in 1931, was signally honored by a meeting of entomologists of the United States Department of Agriculture, the Entomological Society of Washington and the Insecticide Society of Washington on Thursday evening, May 27, to mark his eightieth birthday. Dr. Howard was former chief of the Bureau of Entomology, retiring from office in 1927. The meeting was held in the Entomology Building of the National Research Center at the Beltsville Experimental Farm.

Dr. Howard is famous, not only for the international renown in studies of parasitic hymenoptera (wasp-like insects), but also for his studies of mosquitoes, which began in 1892, several years before the theory that mosquitoes transmit malaria, yellow fever, and other diseases, was generally accepted. When certain mosquito species were identified as disease carriers, Dr. Howard was ready to recommend control measures, particularly the use of kerosene.

The common house-fly also attracted Dr. Howard's attention in the field of medical entomology. His book, "The House-fly—Disease Carrier," published in 1911, is largely responsible for the world crusade against house-fly during the last 25 years. His popular book, "The Insect Menace," published in 1931, awakened wide-spread interest in the dramatic warfare that exists between mankind and the insect world. While optimistic as to the ultimate ability of human beings to retain supremacy over their insect enemies, Dr. Howard in this book focused attention on the need for ever-vigilant measures and a sufficient force of trained entomologists to maintain the continual large-scale control operation necessitated by change in agricultural practices.

Included in the meeting's program were old associates in the Department in the Entomological Society of Washington who spoke informally. A biographical sketch of Dr. Howard was read by F. C. Bishopp and W. R. Walton of the bureau. N. E. McAdoo, President of the Washington Entomological Society paid tribute in a brief address to Dr. Howard's accomplishments.

Dr. W. Calhoun Stirling has returned from an 8-weeks' tour of the principle urological clinics in Europe. He was the guest of Professor Geza Illyes in Budapest, Hungary, where a special clinic was given in his honor. The clinics of Professor Bastanelli in Rome, Hyarnschak in Vienna, Marion, Papin, Chavessu, and Luys in Paris, were also visited.

Members of the Medical Society of the District of Columbia in attendance at Atlantic City at the eighty-eighth annual session of the American Medical Association, June 7–11, 1937:

G. L. Alexander
Victor R. Alfaro
Charles L. G. Anderson
Harry F. Anderson
William P. Argy
Garnet W. Ault
John M. Baber
Wyrth P. Baker
George L. Ball
Anna Bartsch-Dunne
Morris I. Bierman
Abe Blajwas
Joseph B. Bogan
Charles J. Bowne
Thomas Bradley
Earle G. Breeding
Grafton Tyler Brown
Leo T. Brown
Radford Brown
Warren B. Burch
William F. Burdick
John W. Burke
William K. Butler
Edward A. Cafritz
Tomas Cajigas
Charles P. Cake
Ralph J. Carbo
Elma B. Carr
Philip A. Caulfield
John R. Cavanagh
Morris Chase
William W. Chase
Elizabeth E. Chickering
Cline N. Chipman
Roger M. Choisser
William Earl Clark
Thomas A. Claytor
Edith SeVille Coale
J. Lloyd Collins
Coursen B. Conklin
A. J. B. Connolly
Edgar P. Copeland
Karl C. Corley
Allen S. Cross
Jerome F. Crowley
Edward J. Cummings
V. J. Dardinski
A. D. Daughton
David Davis
William DeKleine
Joseph Dessoff
Samuel Dessoff
Philip Diatz
Harry H. Donnally
H. N. Dorman
H. S. Douglas
James H. Earley
Frank J. Eichenlaub
Herman Eisenberg
John H. Elvin
Joseph F. Elward
Ella M. A. Enlows
James W. Esler
Russell J. Fields
James A. Flynn
Thomas M. Foley
Stuart O. Foster
Walter Freeman
L. H. French
Fred A. J. Geier
William T. Gill, Jr.
J. N. Greear, Jr.
Louis S. Greene
Thomas A. Groover
Henry B. Gwynn
Henry G. Hadley
Charles M. Hammett
Irvin Hantman
B. L. Hardin, Jr.
James Hawfield
Ralph J. Haws
W. Preston Haynes
M. Lynwood Heiges
William P. Herbst, Jr.
Myer J. Herschman
Herman Hertzberg
Edmund Horgan
Julian M. Howe
Oscar B. Hunter
Hugh H. Hussey, Jr.
Charles W. Hyde
LeRoy W. Hyde
Merritte W. Ireland (Honorary)
J. Bay Jacobs
Henry W. Jaeger
Fordyce A. H. Johnson
Helen Gladys Kain
S. R. Karpeles
Howard Katzman
Sollie Katzman
Robert A. Keilty
Adam Kemble
Joseph V. Kennedy
Elizabeth A. Kittredge
Maurice J. Kossow
Jacob Kotz
Joseph Kreiselman
D. H. Kushner
Edward Larkin
James P. Leake (Associate)
Thomas S. Lee
Isadore Levin
J. G. Lewis
J. W. Lindsay
Arthur B. Little
John A. Logan
James Alexander Lyon
Henry C. Macatee
Leslie K. MacClatchie
Edward B. Macon
Benjamin Manchester
R. N. Manganaro
Charles C. Marbury
William B. Marbury
Albert E. Marland
Leon A. Martel
Wilbur W. Martin
Lyle M. Mason
Joseph J. McCarthy
F. M. McChesney
G. W. McCoy (Associate)
Charles H. McEnerney
F. X. McGovern
Robert S. McGrath
Joseph J. McHale
Michael J. McInerney
H. J. Russell McNitt
William C. Meloy
Beveridge Miller
William S. Miller
J. Ernest Mitchel
Claude Moore
William A. Morgan
William Gerry Morgan
S. B. Muncaster
Raymond W. Murray
Stephen W. Nealon, Jr.
Lester Neuman
Margaret M. Nicholson
Aaron Nimetz
Edward M. O'Brien
Paul J. O'Donnell
Ella Oppenheimer
William J. B. Orr
Gilbert Ottenberg
K. Elizabeth Parker
J. Winthrop Peabody
Philip O. Pelland
Ivy A. Pelzman
Matthew White Perry
Thomas A. Poole
Maurice Protas
Edgar E. Quayle
Herbert P. Ramsey
William P. Reeves
John C. Reisinger
Frederick A. Reuter
E. Clarence Rice, Jr

Arch L. Riddick
Benjamin Rones
W. Warren Sager
I. Lewis Sandler
Norman P. Scala
H. H. Schoenfeld
Henry R. Schreiber
Mark P. Schultz
Roy Lyman Sexton
Joseph P. Shearer
Elmer R. Shepherd
Ernest Sheppard
Jesse Shoup
Morris Silverman
C. Augustus Simpson
John A. Simpson
Howard L. Smith
Luther H. Snyder
Alma Jane Speer
William Mercer Sprigg
W. Calhoun Stirling
Walter O. Teichmann
Earl R. Templeton
W. D. Tewksbury
E. W. Titus
Frank H. Towner
George B. Trible
John H. Trinder
H. King Vann
J. Russell Verbrycke, Jr.
W. B. Walters
Otto N. Warner
John F. Warren
James C. Waters
James W. Watts
Harry S. Weitzman
R. Lomax Wells
Charles S. White
Eugene R. Whitmore
Oscar Wilkinson
Richard W. Wilkinson
Frank L. Williman
James E. Wissler
Wallace M. Yater
J. Rogers Young
William G. Young

It would appear there was in attendance a total of 212 Active Members representing 26.57 per cent of our active membership. The Society indeed is a subject for congratulation in having this fine representation. The advantages to organized medicine in the United States in having its constituent bodies so thoroughly well represented should be immediately apparent.

The following officers of the American Medical Association have been elected for 1937–1938:

Irvin Abell, Louisville, Ky., *President-elect;* Junius B. Harris, Sacramento, Calif., *Vice President;* Olin West, Chicago, *Secretary;* Herman L. Kretschmer, Chicago, *Treasurer;* Nathan B. Van Etten, New York City, *Speaker, House of Delegates;* Harrison H. Shoulders, Nashville, Tenn., *Vice Speaker, House of Delegates.* The following were elected for the terms indicated: Arthur W. Booth, Elmira, N. Y., and Roscoe L. Sensenich, South Bend, Ind., (terms expire 1942), *Board of Trustees;* J. W. Burns, Cuero, Texas (term expires 1941), *Judicial Council;* Charles Gordon Heyd, New York City (term expires 1944),*Council on Medical Education and Hospitals;* Clyde L. Cummer, Cleveland (term expires 1942), and J. Gurney Taylor, Milwaukee (term expires 1939), *Council on Scientific Assembly.*

Prepare now to attend the eighty-ninth annual session which will be held in 1938 in San Francisco.

American Board of Surgery is Organized. Boards are now in existence for the certification of practitioners of some of the surgical specialties such as ophthalmology, otolaryngology, obstetrics and gynecology, genito-urinary surgery and orthopedic surgery. It is expected that the American Board of Surgery will be responsible for the certification of general surgeons as well as those practicing in the remaining specialized subdivisions of surgery.

The following surgical societies coöperated in the creation of the American Board of Surgery: American Surgical Association, Surgical Section of the American Medical Association, American College of Surgeons, Southern Surgical Association, Western Surgical Association, Pacific Coast Surgical Association and the New England Surgical Society. The first 3 of these bodies which are national in scope have 3 representatives on the Board. All of the other societies have 1 representative each. The representatives of the coöperating societies are nominated by the society which they represent and upon approval of the Board shall become members of it. The term of membership of the Board will be 6 years. The following represent the coöperating surgical societies:

American Surgical Association: Drs. Evarts A. Graham, Arthur W. Elting, Allen O. Whipple; *American College of Surgeons:* Drs. Donald Guthrie, Erwin R. Schmidt, Harvey B, Stone; *Surgical Section of the American Medical Association:* Drs. Fred W. Rankin, Howard M. Clute, J. Stewart Rodman; *New England Surgical Society:* Dr. Philemon E. Truesdale; *Western Surgical Association:* Dr. Thomas Orr; *Southern Surgical Association:* Dr. Robert Payne; *Pacific Coast Surgical Association:* Dr. Thomas Joyce.

Officers: Drs. Evarts A. Graham, *Chairman;* Allen O. Whipple, *Vice Chairman;* J. Stewart Rodman, *Secretary-Treasurer.*

The Board will hold its first examination (Part I, written) on September 20, 1937. All inquiries concerning applications for this examination should be received by the Secretary's office promptly. Requests for booklets of information, application blanks, and other information should be addressed to the Secretary, Dr. J. Stewart Rodman, 225 South Fifteenth Street, Philadelphia, Pa.

NARCOTIC RENEWALS

July 1, 1937

The members of the Society should fulfil the letter of the law governing the prescribing and dispensing of narcotic drugs and preparations such as described in Section 1 of the Act of Congress approved December 17, 1914, as amended.

It is incumbent upon each physician, before July 1 of each year, to make out Treasury Department Form 713, showing the amount of narcotics in their possession and making application for renewal of privilege under the law to prescribe narcotics. A new blank has been arranged this year on which physicians have to state the number of their license to practice medicine in their particular community and further to state the date of issuance of said license. The Medical Society's office has learned of the plight of certain members who have failed to comply with the letter of the law and, therefore, made themselves liable to the penalties under the Act. Avoid all difficulty by making your returns before July 1.

CORRESPONDENCE

The correspondence given below speaks strongly for itself, citing a situation that appears ever present, i.e., of misplaced confidence in door-bell ringers, unauthorized agents. The lesson taught is the making sure by viewing credentials or through other methods of the validity of any claims made by a canvasser. Certainly this should be done before any money is handed out. Remember do not loosen the purse strings until absolutely "shown."

Letter #1—From manufacturer to doctor who apparently lost through credulity.

May 27, 1937.

Dear Doctor:

We received your letter in reference to the order you gave Mr. H. L. Green for garments. Our concern has had no correspondence with Mr. Green for over 3 months. He sold 1 order for us and we have heard nothing from him since, so assume he has represented himself as our agent and taken a deposit with no intention of sending in the order.

We suggest that you get in touch with the Better Business Bureau, and have them send an investigator to get your money back from Mr. Green. As we did not receive these orders, we are forced to assume that he had no intention of sending them in, especially due to the fact that he collected about 3 times the amount of the deposit that any agent is authorized to collect.

We are very sorry for your cost and inconvenience you have been burdened with, but we are in no way liable for the acts of this so-called agent of ours. We are sure the Better Business Bureau will be more than glad to help you out in this matter.

Yours very truly,
WACO GARMENT MFG. COMPANY
L. L. Stroud

Letter #2—Plain statement of Better Business Bureau's position in premises.

June 8, 1937

Dear Doctor:

The Waco Garment Manufacturing Company has somewhat misinformed you about the services of the Better Business Bureau. The Bureau is not in a position to collect deposits and unpaid bills.

Our only record of Mr. H. L. Greene is an earlier complaint against him received last summer, which complaint was of the same character as yours. At that time Mr. Greene's address was 1735-14th Street, N. W.

Several efforts to contact him were quite unavailing.

We are returning herewith your order and the letter you received from the subject.

Yours very truly,
BETTER BUSINESS BUREAU OF WASHINGTON
Joseph W. Marshall, Director

The function of the Better Business Bureau is essentially prophylactic. Unfortunately, it does not seem to function to include the taking care of resultant bad situations. Consultation should be made before and not after any dubious transactions. The above correspondence is revealing.

REPRINTS RECEIVED

The following reprints have recently been received for which due acknowledgment is made:

"The Comparative Adaptability of Pernocton, Avertin and Pentobarbital Sodium for Basal Anesthesia," Joseph B. Bogan, M.D., Anesthesia and Analgesia, May–June, 1933.

"A Clinical Evaluation of Cyclopropane; After Its Use in 300 Surgical Anesthesias," Joseph B. Bogan, M.D., Anesthesia and Analgesia, November–December, 1936.

"Diagnosis of Venereal Diseases: A Study of 4,941 Admissions to a Venereal Disease Clinic," George W. Creswell, A.B., M.D., Southern Medical Journal, December, 1936.

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"A New Bismuth Olive-oil Preparation," Russell J. Fields, B.S., M.D., Urologic and Cutaneous Review, December, 1936.

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"Priority Among American Physicians in Demonstrating the Cause of Grain Itch; Tardy Credit Therefor Given to Dr. Lyman Talmadge Rawles," Herman E. Kittredge, M.D., Journal, American Medical Association, December 26, 1936.

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"The Socialization of Medicine—To What Extent is it Desirable?", Arthur C. Christie, M.D., Journal, Iowa State Medical Society, September, 1936.

"The Present Status of Radiation in the Treatment of Cancer," Arthur C. Christie, M.D., Journal, American Medical Association, September 29, 1934.

"The Diagnosis and Treatment of Carcinoma of the Breast," Arthur C. Christie, M.D., Kansas City Southwest Clinical Society Monthly Bulletin, February, 1936.

"Bronchiectasis: Its Diagnosis and Treatment," Arthur C. Christie, M.D., Radiology, February, 1936.

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"X-ray Treatment in Hyperparathyroidism," E. A. Merritt, M.D., and I. Lattman, M.D., Radiology, June, 1936.

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Equivalent to 5 MM. Copper," E. A. Merritt, M.D., and R. Rhett Rathbone, M.D., American Journal of Roentgenology and Radium Therapy, March, 1936.

"The Treatment of Epithelioma Involving Cartilage Using 220 K.V.P. and Heavy Filtration," E. A. Merritt, M.D., and R. Rhett Rathbone, M.D., Radiology, June, 1935.

"Comparison of the Roentgen and Radium Spectrum From the Standpoint of the Practical Radiation Therapist," R. R. Rathbone, M.D., American Journal of Roentgenology and Radium Therapy, January, 1935.

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"The Treatment of Bacterial Allergy," Grafton Tyler Brown, M.D., The Journal-Lancet, March, 1937.

"The Relief of Labor Pains by the Use of Paraldehyde and Benzyl Alcohol," Howard F. Kane, M.D., and George B. Roth, M.D., Journal, American Medical Association, November 21, 1936.

"Dr. John Gorrie—Inventor of Artificial Ice and Mechanical Refrigeration," George B. Roth, M.D., The Scientific Monthly, May, 1936.

"The Cortical Innervation of Ocular Movements," Ernest A. Spiegel, M.D., and Norman P. Scala, M.D., Archives of Ophthalmology, December, 1936.

"Interstitial Bronchopneumonia in Children," Joseph S. Wall, M.D., The Southern Medical Journal, February, 1937.

"On the Practical Use of the Audiometer," Walter A. Wells, M.D., Virginia Medical Monthly, November, 1936.

BOOKS RECEIVED

Acknowledgment, with thanks, is made of the following books:

Diabetes: A Modern Manual, by Anthony M. Sindoni, Jr., M.D., Chief of the Diseases of Metabolism, St. Agnes Hospital; Chief Consultant in the Diseases of Metabolism, Oncologic Hospital; and Physician to the Medical Dispensary, Presbyterian Hospital, Philadelphia. New York, Whittlesey House, 1937, 240 pp., illustrated. Price $2.00.

Medical Morals and Manners, by Hubert Ashley Royster, M.D., Professor of Surgery, Wake Forest College School of Medicine, Raleigh, N. C. Chapel Hill, The University of North Carolina Press, 1937, 333 pp. Price $2.50.

Man in a Chemical World, by A. Cressy Morrison. New York, Charles Scribner's Sons, 1937, 292 pp., illustrated. Price $3.00.

Carcinoma of the Female Genital Organs, by M. C. Malinowsky and E. Quater, translated from the Russian by A. S. Schwarzmann, A.B., M.D. Boston, Bruce Humphries, Inc., 1936, 255 pp., illustrated. Price $5.00.

Ophthalmoscopy, Retinoscopy and Refraction, With New Chapter on Orthoptics, by W. A. Fisher, M.D., F.A.C.S., Chicago, Ill. Chicago, H. G. Adair Printing Company, 1937, 210 pp., illustrated. Price $2.00.

Senile Cataract: Methods of Operating, by W. A. Fisher, M.D., F.A.C.S., Chicago, Ill. Chicago, H. G. Adair Printing Company, 1937, 150 pp., illustrated. Price $2.00.

Clinical Reviews of the Pittsburgh Diagnostic Clinic. Guideposts to Medical Diagnosis and Treatment, by H. M. Margolis, B.S., M.D., F.A.C.P. New York, Paul B. Hoeber, Inc., 1937, 552 pp.

In the clinical surveys such subjects as undulant fever (brucellosis), agranulocytosis, hypogranulocytosis, carcinoma of the lung, thromboangiitis obliterans, the arthritides, and parathyroid insufficiency are dealt with in a thorough and practical manner. Especially is there placed an emphasis on treatment. A classification of the lymphadenopathies furnishes material for a most interesting chapter. A summarization of experiences in an active diagnostic clinic should afford to the practicing physician an unusual opportunity.

The Cardiac Glycosides. A series of three lectures delivered in the College of The Pharmaceutical Society of Great Britain under the auspices of the University of London, by Professor Arthur Stoll, D.Sc., M.D. London, The Pharmaceutical Press, 1937, 80 pp., illustrated.

In a succinct although complete manner the basic as well as the more recently acquired information concerning the glycosides of *Digitalis purpurea*, *Digitalis lanata*, squill, and *Strophanthus* are dealt with in a series of 3 lectures.

Principles and Foibles of Cancer Research in Regard to Etiology and Nature, by William Rienhoff, Sr., M.D., F.A.C.S. Baltimore, Waverly Press, Inc., 1936, 200 pp.

George Mendenhall Ruffin
(1876-1937)

Dr. George M. Ruffin, a member of the Medical Society of the District of Columbia since April 4, 1906, died on Saturday, May 29, 1937. His seniority number in the Society was 406. From time to time he had committee appointments; his last assignment was on the Legal Advisory Committee of 1927. He was graduated in medicine from the George Washington University School of Medicine in 1902. His extensive practice was limited to his specialty, internal medicine. Dr. Ruffin was born in Wilson, N. C., the son of Dr. John Kirkland Ruffin and Mrs. Sarah Tayloe Ruffin. His paternal grandfather, Thomas Ruffin, served for years as Chief Justice of the State of North Carolina. He is survived by his widow, Mrs. Bessie Draper Ruffin; a daughter, Barbara; two brothers, Dr. Sterling Ruffin, and Thomas Ruffin; and a sister, Mrs. William B. Sims. Funeral services were held in Washington on Tuesday, June 1, following which his body was cremated. Later his ashes will be interred in the family plot in the cemetery of St. Matthew's Episcopal Church, Hillsboro, N. C.

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CHEMICOBIOLOGICAL AND CLINICAL BEHAVIOR OF ARSENOXIDE (MAPHARSEN)*

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The arsenical preparation meta-amino, para-hydroxy, phenylarsenoxide, or as it is more commonly termed by laboratory workers "arsenoxide," was largely a laboratory curiosity in the United States until Tatum and Cooper, about a half decade ago reinvestigating its effect in rat trypanosomiasis and rabbit syphilis, found that although it was relatively ineffective in trypanosomiasis, it possessed a therapeutic index in rabbit syphilis higher than that of any other antisyphilitic agents which they had tried in the laboratory. They were convinced by their findings that arsenoxide "has such outstanding advantages over the arsphenamines as to entirely justify a clinical investigation of the compound."

This suggestion of Tatum and Cooper was carried out by Foerster and his associates, who, employing arsenoxide in human syphilis and after a study covering a period of 18 months and the use of about 5,000 injections in over 200 cases, reported that the visible lesions healed as rapidly and as completely as they did under the arsphenamines, the Wassermann reaction being reversed in nearly all early cases, with relapse in only about half the cases. They further reported that nitritoid reactions did not occur and that the immediate symptoms suggestive of a toxic action were those resembling mild irritation of the gastro-intestinal tract. However, jaundice and renal impairment were present in 4 cases.

Foerster's paper was soon followed by a number of others, among them being those of Gruhzit and his associates of the research laboratories of Parke, Davis & Company, who have made both laboratory and clinical studies with the compound. Their conclusions were rather far-reaching, among which was the statement that arsenoxide "is a safer drug" and causes less severe complications than the arsphenamines; moreover, "its therapeutic effectiveness appears equal to or higher than neoarsphenamine."

Shortly after the report of Gruhzit a paper by Raiziss and Severac appeared which practically duplicated the work of Gruhzit, in which it was shown that neoarsphenamine was considerably more efficient than arsenoxide both in trypanosomiasis and rabbit syphilis. They concluded that since the clinical curative dose of arsenoxide in rabbit syphilis was practically identical with the lethal dose, the clinical use of the compound in adequate curative doses might be fraught with considerable danger.

Since considerable clinical evidence had accumulated which seemed to justify the conclusion that the product should be made available for general therapeutic use, it was accordingly placed on the market and has since been accepted for inclusion in "New and Nonofficial Remedies" by the Council of Pharmacy and Chemistry of the American Medical Association under its abbreviated chemical name Mapharsen. A patent for the commercial product has been asked for in the United States.

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* Read before the Annual Scientific Assembly of the Society, May 6, 1937.

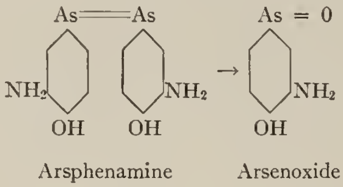
CHEMICAL STRUCTURE

Arsenoxide is a trivalent arsenic compound that is closely related to the arsphenamines, differing structurally from the latter chiefly in its molecular size. It is formed from any of the arsphenamines whenever they are oxidized. This breakdown may readily occur from the arsphenamines when they are in alkaline solution, either in vitro or vivo.

If one generically represents the arsphenamines by the formula R. As = As. R, in which R represents the phenyl residue with its active amino group in the meta position and its hydroxyl group in the para position, its decomposition product, arsenoxide, is symbolized by the shortened formula, R. As = 0.

Their structural relationship is more clearly shown by the following chart:

ARSPHENAMINE-ARSENOXIDE RELATIONSHIP



The commercial product is dispensed as the hydrochloride, a form which is readily soluble in water, forming an acid solution. However, each ampule of the commercial product contains in addition to the arsenoxide hydrochloride, definite amounts of sodium carbonate and anhydrous sucrose in order to make the solution practically neutral and isotonic with the blood when given as a 0.6 per cent solution.

Effervescence occurs upon the addition of water to the powdered Mapharsen mixture due to the interaction between the added carbonate and the acid group of the molecule.

Effervescence being completed, no further procedure is necessary to prepare a solution properly for intravenous use, except to bring it to a dilution of 0.6 per cent with distilled water.

Mapharsen is protected from decomposition while in ampule by being sealed in an atmosphere of nitrogen.

Arsenoxide hydrochloride has a wide range of solubility, being soluble in water, acids, alkalies and alkali carbonates. It is probable that arsenoxide also exists in the blood in solution. Arsphenamine hydrochloride on the other hand, while soluble in water, is insoluble in alkalies, the precipitate redissolving in excess of the alkali. For example, Elvove and Clark found that arsphenamine hydrochloride began to precipitate when 1 mol of normal sodium hydroxide was added, or at a pH of about 3, and that it would not begin to redissolve until 3 mols were added, or at a pH of about 10, so that at the pH of the blood, which is about 7.3, arsphenamine likely exists in the blood in the form of a precipitate or a complex colloid.

BEHAVIOR OF ARSENOXIDE TOWARD BLOOD PROTEINS

It is a well-known fact that acid solutions of arsphenamines in concentrations of 0.25 per cent or more will flocculate serum in vitro, whereas neoarsphenamine in as high a concentration as 40 per cent will cause none (Schamberg, et al.).

From a priory reasoning one would expect that the acid solution of arsenoxide hydrochloride should behave like the acid solution of arsphenamine; but this is not the case. We have found that while there is a slight increase in the turbidity of blood serum when equal quantities of 0.6 per cent arsenoxide hydrochloride and serum are added to each other, the serum remains translucent and does not settle upon standing. We have further found that when either the commercial arsenoxide (Mapharsen) or an alkalinized experimental sample of arsenoxide hydrochloride was employed, no increase in the turbidity of blood serum or settling was present after standing for hours.

Gruhzit states that arsenoxide (presumably the hydrochloride) is not precipitated by tissue fluids nor does it cause either agglutination or hemolysis in concentrations of from 0.6 to 1 per cent. On the other hand Schamberg and his collaborators reported that both acid and alkaline solutions of arsphenamine were strongly hemolytic for defibrinated blood in all concentrations. From these observations one should expect arsenoxide to cause few or very minor symptoms of an anaphylactoid type upon its intravenous injection.

TABLE 1

DIFFUSION DEPTH OF ARSENOXIDE IN 5 PER CENT GELATIN (ROOM TEMPERATURE)

COMPOUND	EXPERIMENT 1 AFTER 20 HOURS	EXPERIMENT 2 AFTER 24 HOURS	EXPERIMENT 3 AFTER 17 HOURS
Picric Acid, 0.5 per cent	18 mm.	23 mm.	18 mm.
Copper Sulphate, 0.5 per cent	20 mm. (As 5 per cent)	14 mm.	12 mm.
Arsphenamine, 0.5 per cent	Acid 1 mm. Alk. 1 mm.	Acid 2 mm. Alk. 4 mm.	Acid 3 mm. Alk. 6 mm. (Both 2 per cent Sol.)
Arsenoxide Lab. No. 2, 0.5 per cent	Acid 10 mm. Alk. 10 mm.	Acid 20 mm. Alk. 25 mm.	Acid 12 mm. Alk. 15 mm.
Mapharsen, 0.5 per cent		35 mm.	
Neoarsphenamine, 0.5 per cent	2 mm.	4 mm.	

TABLE 2

TOXICITY OF "ARSENOXIDE" FOR RATS, ADMINISTERED INTRAVENOUSLY*

SAMPLE	NUMBER OF RATS USED	DOSE	DIED	LIVED	COMMENT
		mg. per kg.	*per cent*	*per cent*	
Lab. No. 1. Arsenic, 27.4 per cent	5	10	0	100	Given as sodium salt. M.L.D. = 20 mg. per kilo
	5	15	40	60	
	5	20	60	40	
	5	30	100	0	
Lab. No. 2. Arsenic, 29 per cent	4	15	0	100	Given as sodium salt. M.L.D. = 20 mg. per kilo
	4	20	100	0	
	4	25	100	0	
Lab. No. 2. Arsenic, 29 per cent	4	10	0	100	Given as acid solution. M.L.D. = 20 mg. per kilo
	4	15	25	75	
	4	20	75	25	
Mapharsen. Arsenic, 29 per cent	8	15	0	100	M.L.D. = 25 mg. per kilo
	12	20	33	66	
	12	25	100	0	

* M.L.D. = dose killing 60 per cent or more.

DIFFUSIBILITY OF ARSENOXIDE

Solutions of arsphenamine and neoarsphenamine behave as semicolloids (Voegtlin), the size of the aggregates diminishing from acid arsphenamine, through alkaline arsphenamine and neoarsphenamine. From this fact alone one may, therefore, expect the immediate reactions to be more marked from the former, and slight from the latter, with alkaline arsphenamine showing an intermediate type of reaction, expectations which have been fully realized in their clinical use.

Since the acute effects of arsenoxide are slight after its intravenous administration, it appeared to us that arsenoxide should not be regarded as a semicolloid. To test our hypothesis diffusion experiments were carried out with 5 per cent gelatin, in which arsenoxide was compared with arsphenamine and neoarsphenamine, and it was found that arsenoxide, either as the acid or alkaline solution (NaOH), diffused readily and to a marked degree within 24 hours, thus closely resembling the diffusibility of picric acid and copper sulphate, which were used as representatives of the class of crystalloids. On the other hand, arsphenamine and neoarsphenamine showed little or no diffusion during a similar period of time. The results of these studies are shown in Table 1.

TABLE 3

Toxicity of Arsenoxide After Exposure to Oxygen, Administered Intravenously to Rats

SAMPLE	NUMBER OF RATS USED	DOSE	DIED	LIVED	COMMENT
		mg. per kg.	*per cent*	*per cent*	
Mapharsen. Arsenic 29 per cent.	4	15	0	100	Given as a 0.6 per cent solution; slightly acid to litmus
	4	20	25	75	
	4	25	100	0	
	After shaking the solution in air for 15 minutes				
	4	25	100	0	Shows no decrease in toxicity
	After bubbling air through the solution for 2 hours				
	4	15	0	100	Shows an apparent but slight increase in toxicity
	4	20	75	25	
	4	25	75	25	
	After exposure of the solution to air for 2 months				
	4	30	0	100	Shows a decrease in toxicity

ACUTE TOXICITY OF ARSENOXIDE

The toxicity of arsenoxide* was ascertained on rats by administering it intravenously according to the National Institute of Health method for testing for the toxicity of the arsphenamines, the single dose which would kill 60 per cent or more of the animals within 48 hours being regarded as the minimal lethal dose.

Three samples of arsenoxide were tested in this manner, 2 being laboratory and 1 a commercial sample. As shown in Table 2, it was found that the maximal tolerated dose was 15 milligrams per kilogram of body weight for each of the laboratory samples and 20 milligrams for the commercial sample, while the minimal lethal dose for each of the laboratory samples was 20 milligrams, and for the commercial sample 25 milligrams per kilogram of body weight.

Our toxicity figures agree very closely with those obtained by other recent observers (Tatum and Cooper; Gruhzit; Raiziss and Severac). They are somewhat lower than those obtained by Ehrlich and Hata. It is not improbable that these earlier observers worked with a product of lesser purity than that of more recent origin.

We have not discovered the reason for the different values obtained for our laboratory and the commercial product, but it does not appear to be due to the variation in the reaction of the solutions, since from Table 2 it will be seen that laboratory sample 2 possessed the same toxicity when given either as the acid or alkalinized solution.

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* Samples were kindly supplied by Dr. Oliver Kamm of the Parke, Davis Laboratory, Detroit, Mich.

This finding is in striking contrast to our results, previously reported for arsphenamines (Roth), when it was shown that a 1 per cent acid solution was 4 times as toxic as a 2 per cent alkalinized solution of arsphenamine.

Another essential difference in the chemico-biological behavior of arsenoxide from that of the well-known arsphenamines, arsphenamine and neoarsphenamine, is that solutions of these arsphenamines have been found to increase in toxicity markedly on exposure to the air (Roth), whereas when a solution of arsenoxide is exposed to the air for varying periods, it essentially shows a decrease in toxicity, as will be seen from Table 3.

Symptoms in Rats After Arsenoxide

The symptoms produced in rats after the intravenous administration of arsenoxide are largely immediate and rather striking.

The effects of small doses, up to 5 milligrams per kilogram of body weight, are slight, the animals showing a mild degree of salivation and lacrimation, moderate weakness and dyspnea, with recovery after about ½ to 1 hour.

When the dosage range is extended to from 10 to 25 milligrams per kilogram of body weight, most of the animals immediately become severely ill and remain so for about an hour, the symptoms being marked salivation and lacrimation, ineffective retching attempts, marked dyspnea and weakness, and occasionally diarrhea. Following this period of acute illness, recovery occurs unless a lethal dose has been given, when death takes place after from 1 to 6 hours, sometimes following a convulsion. Only 2 of our animals died after the sixth hour, death in both cases being at the end of a week. Cannibalism prevented necropsy on 1 animal; the other presented a pale contracted kidney at necropsy.

Similar toxicity studies were made on rats in which we compared arsenoxide with arsphenamine, neoarsphenamine and sodium arsenite, comparing them in terms of both the compound and their arsenic content. Our results will be found in Table 4.

In terms of the compound itself, arsenoxide is shown to be somewhat less toxic than the inorganic trivalent arsenical, sodium arsenite, whereas in terms of their content of arsenic they are about equal in toxicity. Arsenoxide, however, is many times more toxic than arsphenamine or neoarsphenamine when compared in either manner, it being about 6 times as toxic as arsphenamine and 10 times as toxic as neoarsphenamine on the basis of their arsenic content.

It has appeared questionable to some whether such an extremely toxic compound as arsenoxide should be used in therapeutics. In the consideration of such a question one must take into account not only initial toxicity, but whether it produces side-effects; and, finally, one should determine the relation of its toxicity to its therapeutic efficiency, or, in the language of the laboratory investigator, its therapeutic index.

Unfortunately there is no agreement among investigators as to the therapeutic index of arsenoxide, as will be concluded from Table 5. In the last analysis the therapeutic efficiency of a compound can be determined only by its clinical exhibition. At the present time the usual clinical dosage of neoarsphenamine is 0.6 gram; of arsphenamine, 0.4 gram; and of arsenoxide, 0.060 gram, which on the basis of their arsenic content would be: neoarsphenamine, 120 mg.; arsphenamine, 120 mg.; arsenoxide, 18 mg. Thus, one clinically gives about one seventh the amount of arsenic as arsenoxide as when giving the arsphenamines. Since from Table 4 we have shown that the relative toxicity of arsphenamine to arsenoxide on an arsenic content is 10 to 1.6, that is, 6.3 to 1, and since the clinical dose ratio is 7 to 1, the therapeutist using a dose of 60 mg. of arsenoxide may be considered to be proceeding rationally and assuming no greater risk than he does when using the arsphenamines.

Parasiticidal Activity of Arsenoxide

It was early shown by Ehrlich and Hata that the arsphenamines had little or no effect upon protozoal parasites in the test tube, while in the body they were highly destructive, findings which have been confirmed by every later investigator in this field.

In 1920 Voegtlin and Smith advanced the theory that the parasiticidal activity of the arsphenamines in the body was due to the formation of the decomposition product, arsenoxide. Moreover, they were able to show from their experiments in rat trypanosomiasis that the destructive effect began after a latent period, whereas after arsenoxide the action began at once.

A few years later Voegtlin, Dyer and Leonard found that the rat trypanosome with which they worked was inactivated by practically the same concentration of arsenoxide in the body as in the test tube, thus lending additional support to the theory previously advanced that the arsphenamines acted through their decomposition into arsenoxide.

It remained for Rosenthal, in 1932, to devise a test for the differentiation of arsenoxide from the arsphenamines both in vitro and vivo, and by it he was able to show that about 10 to 12 per cent of the arsenoxide could be recovered from the liver of the rat after 3 to 4 hours. None was to be found in any of the other tissues. Following the injection of neoarsphenamine, arsenoxide could be recovered only from the kidneys, the concentration in this organ being comparable to that found in the liver after arsphenamine.

The laboratory studies on the parasiticidal activity of arsenoxide fall into 2 periods, an early and recent, the early dealing mainly with its effect on rat trypanosomiasis, the recent with both trypanosomiasis and rabbit syphilis.

From an examination of Table 5 it will be found that against rat trypanosomiasis (T. equiperdum) arsenoxide was found to be less effective than either arsphenamine or neoarsphenamine. Against rabbit syphilis, however, Tatum and Cooper, and Gruhzit found arsenoxide to be slightly more effective than neoarsphenamine, while on the other hand Raiziss and Severac found it to be only one fifth as active. There are thus seen to be 2 widely divergent views held regarding the efficacy of arsenoxide in rabbit syphilis.

TABLE 4

TOXICITY OF MAPHARSEN, ARSPHENAMINE, NEOARSPHENAMINE AND SODIUM ARSENITE, FOR RATS, ADMINISTERED INTRAVENOUSLY*

COMPOUND	NUMBER OF RATS USED	DOSE	DIED	LIVED	M.L.D. IN TERMS OF		RELATIVE TOXICITY OF ARSENIC
					Compound	Arsenic	
		mg. per kg.	*per cent*	*per cent*	*mg.*	*mg.*	
Mapharsen. Arsenic, 29 per cent	8	15	0	100			
	12	20	33	66			
	12	25	100	0	25	7.3	10
Arsphenamine No. 2. Arsenic, 30 per cent	5	120	0	100			
	10	140	30	70			
	10	160	100	0	160	48	1.6
Neoarsphenamine D. Arsenic, 19 per cent	10	280	10	90			
	10	320	50	50			
	10	400	90	10	400	76	1
Sodium arsenite. Arsenic, 54 per cent	5	7.5	0	100			
	5	10	80	20	10	5.4	14
	5	15	100	0			

* M.L.D. = dose killing 60 per cent or more.

DISTRIBUTION, EXCRETION AND ORGANOTROPIC EFFECTS OF ARSENOXIDE

Inasmuch as the effects of a chemical agent on an organ are usually found to be proportional to the concentration of the substance or its decomposition product in that organ, it is informative to determine both its distribution and elimination by quantitative methods.

Considerably more work has been done on the excretion of arsphenamine and neoarsphenamine than on arsenoxide. Voegtlin and Thompson found that only 20 per cent of the arsenic of arsenoxide was excreted by the urine and feces in the white rat in 24 hours, although it had disappeared rapidly from the blood.

Gruhzit and Dixon, working with dogs, found that after the use of Mapharsen 40 to 45 per cent was eliminated in the urine and 55 to 60 per cent in the feces, a total of 65 to 95.5 per cent being eliminated in 1 week. The liver and kidneys were found to contain about equal amounts of arsenic. They also state that the retention of arsenic in the various organs and tissues is from one tenth to one twentieth as great as that observed after arsphenamine or neoarsphenamine.

TABLE 5

Efficiency of Arsenic Compounds in Rat Trypanosomiasis and Rabbit Syphilis when Injected Intravenously*

OBSERVER	COMPOUND	TRYPANOSOMA EQUIPERDUM			TREPONEMA PALLIDUM		
		M.L.D.	M.E.D.	Therap. Index	M.L.D.	M.E.D.	Therap. Index
Voegtlin and Smith, 1920	Arsenoxide	10†	0.75	13			
	Arsphenamine	75†	2	37			
	Neoarsphenamine	100	3	33			
		M.T.D.	M.C.D.		M.T.D.	M.C.D.	
Tatum and Cooper, 1934	Arsenoxide	20	0.8	25	10	6	1.7
	Neoarsphenamine	325	8	41	200	180	1.1
Gruhzit, 1935	Arsenoxide	18	2	9	8	2	4
	Neoarsphenamine	200	24	8.3	Figures not stated		3.75
Raiziss and Severac, 1935	Arsenoxide	18	2.5	7.2	11	12	0.92
	Neoarsphenamine	400	20	20	200	40	5

* M.L.D. = Minimal lethal dose.
M.T.D. = Minimal tolerated dose.
M.E.D. = Minimal effective dose.
M.C.D. = Minimal curative dose.
† On arsenic basis.

These observations indicate that the excretion of the arsenic in arsenoxide occurs in a manner different quantitatively from that of arsphenamine and neoarsphenamine.

Bulmer followed the excretion of the arsenic of arsphenamine in dogs after its intravenous administration and found that while the rate and amount excreted in the urine and feces varied greatly, more was excreted in the feces than in the urine and that by tying off the common bile duct, the excretion was greatly lessened, being practically the same in amount as that excreted in the urine. Thus he showed that the arsenic found in the feces came mainly from the liver through the bile and not by being excreted through the intestine.

These findings of Bulmer on dogs have been duplicated and added to by Underhill and Davis in man. They found that after the clinical use of arsphenamine or neoarsphenamine intravenously, more arsenic was excreted in the feces than in the urine, but that in the case of neoarsphenamine the excretion in the urine greatly exceeded that after arsphenamine.

Although Gruhzit and Dixon found that the arsenic of arsenoxide was excreted about equally in the feces and urine and that the liver and kidneys contained about equal amounts of arsenic, the damage to the liver was not severe, whereas the kidneys were severely damaged, especially in the region of the convoluted tubules.

Gruhzit had shown previously that both rabbits and dogs died after some days from the effects of kidney damage.

Hooper and his collaborators made a quantitative comparison of the effects of arsenoxide, arsphenamine and neoarsphenamine on the rat kidney, and found that while the lesions resembled each other qualitatively, arsenoxide on an arsenic basis was 5 times more toxic to the kidney than neoarsphenamine and 7½ times more toxic than arsphenamine. In the dog they found more pronounced liver changes after arsphenamine than after neoarsphenamine.

Kolmer and Lucke, working with rats exclusively, also showed that arsphenamine had a tendency to produce liver injury and neoarsphenamine kidney injury, thus verifying the findings of Hooper and his collaborators.

We may thus regard the liver as the main arsenic clearance depot for arsphenamine, and the kidney for neoarsphenamine, while for arsenoxide both the liver and kidney share about equally in its excretion. These findings may reasonably be used to explain the relatively frequent occurrence of liver damage after arsphenamine and kidney damage from neoarsphenamine after their clinical use.

It also affords an explanation for the rather severe kidney damage found after arsenoxide but does not indicate a reason for the absence of liver damage after it. The relatively frequent occurrence of gastro-intestinal disturbances after arsenoxide suggests that more arsenoxide is excreted directly into the gut than through the liver by way of the bile.

We have nothing of importance to add to those findings of previous workers relative to the pathological changes produced by arsenoxide in rats except that we have found hydrothorax to be a regular finding in all animals dying after an acutely lethal dose. The amount of a clear serum-like fluid in the thoracic cavity is large (3 cc.), as the figures in Table 6 will show.

We are now investigating this phase of the action of arsenoxide and shall make it the subject of a later report. It is not unlikely that the immediate symptoms present in rats are due to pulmonary changes that are secondary to circulatory disturbances.

Clinical Toxicity and Probable Value of Arsenoxide in Syphilis

The clinical toxicity of a drug is necessarily modified by the disease itself, so that a chief requisite for successful arsenic therapy in syphilis is a knowledge of what structures are mainly involved and the extent of the existing damage to them.

Complications and reactions from the use of an arsenical, therefore, should not always be ascribed to the drug but may be caused by its injudicious use.

It is our belief that many reactions following arsenical therapy may be avoided by a careful study of the patient and judicious selection of the drug. Occasionally, however, despite all precautions, reactions will occur, which for want of a better term are placed under the head of idiosyncrasy, or, in other words, hypersusceptibility.

TABLE 6

Fluid in Thoracic Cavity After Mapharsen Given Intravenously to Rats as 0.6 Per Cent Solution

RAT NUMBER	WEIGHT	DOSE	REACTION SOLUTION	THORACIC FLUID	TIME LIVED
	grams	*mg. per kg.*		*cc.*	*minutes*
51	133	15	Acid	2.8	245
32	154	20	Acid	4.5	65
47	149	20	Acid	1.5	65
37	160	20	Alkaline	3.3	100
38	153	20	Alkaline	2.8	183
39	163	20	Alkaline	3.3	190
40	170	25	Alkaline	2.5	188
41	169	25	Alkaline	1.8	128

We have administered arsenoxide in the form of Mapharsen in a small series of 32 outpatients with syphilis, most of whom had reactions from the arsphenamines, such as marked nausea, vomiting and diarrhea, jaundice, and nitritoid crises. The drug was given intravenously as a 0.6 per cent solution, the administration being rapid, as directed by the dispensing manufacturer.

The initial dose was 0.03 gram for females and 0.04 gram for males, followed by weekly injections of 0.04 gram for females and 0.06 gram for males until 10 treatments were received.

It was found that the drug was better tolerated than the arsphenamines in 20 of our 32 patients. Of the remainder, 9 patients reacted as severely or more markedly than after the arsphenamines, all of them presenting the gastro-intestinal type of reaction. In most cases in which arsphenamines had caused nausea and vomiting 4 to 6 hours following the injections, Mapharsen not only caused nausea and vomiting but moderate to severe diarrhea.

All of the patients who showed jaundice from arsphenamine were not jaundiced after the use of Mapharsen.

In 3 cases of ocular syphilis the results were excellent. Two of these cases were previously jaundiced after the use of arsphenamine but showed none after the use of Mapharsen. The third case with interstitial keratitis had been receiving neoarsphenamine with no apparent improvement. The maximum dose of Mapharsen (0.06 gram) was given with clearing of the cornea almost at once. However, there was nausea, vomiting and diarrhea of the progressive type.

In 12 patients in whom arsphenamine caused mild to severe nitritoid crises, Mapharsen caused no immediate reaction of this type.

All of the 32 patients who received Mapharsen complained of a burning sensation in the arm and shoulder, even though the drug was administered rapidly, as directed. This symptom disappeared promptly, particularly when the patient was reassured and told that the pain was of no consequence.

In no case was sclerosis of a vein noted.

Summary and Discussion

The data obtained from our clinical studies are in no manner conclusive; however, from the laboratory viewpoint we have found arsenoxide to resemble the crystalloidal type of arsenical. It is not only more readily diffusible than the arsphenamines but unlike the latter, possesses a wide range of solubility, being soluble in water, serum, acids and alkalis. It is highly likely that it exists in the blood in solution. The fact that it does not produce the distressing type of nitritoid crisis is most probably due to its crystalloid-like nature, together with its ready solubility in the body fluids.

Arsenoxide is a substance in vitro relatively stable toward oxidative influences and does not materially increase in toxicity, if any, under such conditions; on the other hand, a slow decrease occurs.

Although its acute toxicity is about as high as sodium arsenite, that is, about 6 times as toxic as arsphenamine, its clinical efficiency on an arsenic basis is about 6 times as great. The therapeutist, therefore, need use a dose only one sixth as large as the arsphenamine dosage, a ratio which has been found to be workable in its clinical use.

The excretion of arsenoxide differs from the arsphenamines, essentially in that the excretion of the former is about equally divided between the intestines and the urine, whereas in the case of arsphenamine it is largely by way of the intestines (through the liver), a much smaller amount being found in the urine than feces. This is also true for neoarsphenamine, except that relatively more of it is excreted in the urine than is the case with arsphenamine.

Experience in both the laboratory and clinic has shown that neoarsphenamine is prone to affect the kidney. In this respect arsenoxide resembles it, but the tendency of the latter to produce gastro-intestinal disturbances suggests that relatively more of the arsenic of arsenoxide is excreted directly through the wall of the gastro-intestinal tract than of the arsphenamines.

Our preliminary clinical studies indicate that arsenoxide is a potent drug in clinical syphilis and may be especially useful in cases in which the arsphenamines are not well tolerated, particularly in those cases in which nitritoid crises and jaundice have occurred after their exhibition.

We do not regard the pain in the arm and shoulder distressing enough to be of special significance. It is more likely that the extensive use of arsenoxide will be hindered by its ability to produce gastro-intestinal symptoms and kidney injury.

If one is to be guided by the history of other new drugs, we may conclude that further clinical experience may disclose limitations and side actions, as well as advantages, not now recognized. The product seems to be safe, as well as efficient, when properly used, and since the accumulated clinical reports after over a million administrations are generally favorable, it is exceedingly likely that it will become generally recognized as one of the approved agents in antisyphilitic therapy.

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Insulin Hypoglycemia in the Treatment of Schizophrenia. I. General Considerations. . . . In March, 1936, we discovered, quite by accident and before becoming aware of similar work that was being done in Europe, that dementia praecox patients were usually resistant to very large doses of insulin, and to hitherto unknown extremes of hypoglycemia; that, when they were finally given a dose which produced shock, the psychotic condition improved; and that, when such shock was oft repeated, complete remission occurred in from 6 weeks to 3 months in most cases. . . .

Observations.—1. We have found several patients who could take 200 units of insulin at a dose repeatedly and show no signs of shock. We call these individuals insulin-sensitive, but they are not strictly that, because we have commonly found their blood sugar to be below 20 mg. per 100 cc. (and as low as 3 mg.) when they showed no evidence of shock. . . .

2. One of the first things we observed was that hypoglycemic shock is not due to hypoglycemia. Many patients will maintain a blood sugar level between 15 and 20 mg. per 100 cc. for several hours and show only mild symptoms, such as sweating, hunger, pallor, and anxiety, and then go into shock while the blood sugar level is rising. We think that the cause of shock is hypoglyhydria (a more expressive and more convenient term than hypoglycorrhachia). . . .

3. Blood Sugar/Spinal Fluid Sugar Ratio. There is a wide variation in what various investigators have found to be the normal spinal fluid sugar level; however, most of these opinions range from 20 to 40 mg. lower than the blood sugar. This would make the ratio somewhere between 10/8 and 10/6, or between 1.25 and 1.66. Our studies show that this ratio is completely reversed in the first hour, sometimes the first half hour, after insulin is given, and this inverted ratio is maintained until sugar is administered. In 43 such observations . . . ., at half-hour intervals, this phenomenon has occurred in all but one instance.

4. Spinal Fluid Pressure and Blood Pressure. . . . As the blood sugar falls, spinal fluid pressure rises rather sharply, sometimes increasing as much as 400 mm. of water, but it nearly always begins to fall sometime before, and is usually at the pre-treatment level by the time shock ensues. . . .

Comment.—We think that this method is a definite advance in the treatment of dementia praecox because the percentage of spontaneous remissions under former methods of handling is only from 15 to 30 per cent and they occur only after many months, whereas we have had 63.8 per cent of total remissions, and improvement sufficient to enable the patient to return to his environment and activity, and most of these remissions occurred in from 6 to 10 weeks. While our group of cases is not large, it is large enough to rule out the element of mere chance, because chance is never so consistent. It cannot be denied that the treatment has produced definite results. In the first group of 30 cases we reported, 73.3 per cent were thus improved, 60 per cent having had complete remission. Then we began all manner of experimentation to discover explanations for the various phenomena seen, to simplify the treatment and make it safer, and to devise a modification that could be used on a large scale in large state hospitals. Since that our percentage of good results has not been so high.

Of course it is impossible to estimate how long the recovered patients are going to stay well until many years have passed, but if they can recover from an attack in from 6 to 10 weeks and remain well for 4 or 5 years and then repeat the process, it will still leave a much better control over the situation than we were ever able to gain before.

We consider that the treatment has been put on a definitely safe basis. We have had no deaths and only 1 serious accident, which was a case in which the reaction went too deep and could not be terminated by large and frequent quantities of sugar, both by tube and by vein. This proved to be a case of severe alkalosis with hyperventilation and was relieved by rebreathing, 120 grains of ammonium chloride, and a small dose of morphine to relieve the respiratory stimulation.

The technique is not foolproof by any means and requires skill and judgment which can be acquired only by experience. It is our aim to develop a technic that is applicable to large state hospitals which have many such cases and very limited personnel. . . .

Abstract from article by G. W. Day, M.D., and E. O. Niver, M.D. Galveston, *Texas State Journal of Medicine, July, 1937, p. 236.*

THE PRESENT STATUS OF MAPHARSEN IN THE TREATMENT OF SYPHILIS

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Just 4 decades ago Sir William Osler defined syphilis as "a specific disease of slow evolution, propagated by inoculation (acquired syphilis) or by hereditary transmission (congenital syphilis)." As to its etiology, he wrote, "the nature of the virus is still doubtful . . . syphilis is peculiar to man, and cannot be transmitted to the lower animals." The present-day therapeutic attack on the pathological picture resulting from infection with the Treponema pallida utilizes many new drugs developed since Osler made the following comment on the treatment of syphilis: "The treatment of the disease is now practically narrowed to the use of 2 remedies, justly termed specifics, namely, mercury and iodide of potassium. The former is of specific service in the secondary, the latter in the tertiary manifestations of the disease; but they are often combined with advantage. . . . In the treatment of the visceral lesions of syphilis, iodide of potassium is of equal or even greater value than mercury. Under its use ulcers rapidly heal, gummatous tumors melt away, and we have illustration of a specific action only equalled by that of mercury in the secondary stages, by iron in certain forms of anemia, and by quinine in malaria." Mercury was prescribed in 1-grain pills of hydrargyrum cum creta (gray powder) to be taken orally 4 to 6 times a day for months, by inunction (the preferred route), by intramuscular injection of $\frac{1}{3}$ grain of the bichloride in 20 minims of water once a week, or by fumigation through the volatilization of calomel.

Forty years have elapsed since Osler wrote the above. Mercury and iodide of potassium have stood the test of time, but in that time many new landmarks of progress in the diagnosis and treatment of syphilis have been established. Among these landmarks of progress are the demonstration by Metchnikoff and Roux in 1903 that certain anthropoid apes were susceptible to syphilis; the discovery of the spirochete in 1905 by Schaudinn and Hoffman; the introduction into the field of diagnosis of the serum reaction of Wassermann, and the development of arsphenamine, neoarsphenamine, silver arsphenamine, tryparsamide, bismuth and refinements in mercury administration as useful agents of therapeusis. More recently, a refinement in arsenical therapy has been presented to the profession in the form of meta-amino-para-hydroxyphenylarsine, a trivalent arsenical identical with arsenoxide, and designated by Tatum and Cooper as Mapharsen.

Mapharsen has not been definitely and finally established or proved as equal or superior to any or all of the intravenous arsenicals now accepted and used in the treatment of syphilis, since its clinical application has been comparatively too recent. However, experimental laboratory work and sufficient clinical trials have shown it to have a place in our antisyphilitic therapeutic armamentarium. This is evidenced by its acceptance by the Council on Pharmacy and Chemistry of the American Medical Association and more recently by its inclusion among the acceptable drugs to be used in the treatment of syphilis by the Committee on Treatment of the recent Conference on Social Diseases held here in Washington at the request and under the direction of Surgeon General Thomas Parran. Its real and relative value must be based on the percentage of infectious relapses occurring following its use in the treatment of the primary and secondary manifestations of the disease; the percentage of Wassermann reversals and negative dark-field examinations, and 5, 10 and 15 years hence the results in patients now being treated with Mapharsen which can be studied in the light of the incidence of the latent manifestations of the disease, such as cardiovascular and central nervous system involvement, as compared with the results obtained by the other arsenicals now in common and accepted use. On the basis of the percentage of infectious relapses the consensus of opinion is that Mapharsen ranks along with neoarsphenamine. Experience has shown that the effectiveness of an arsenical in preventing infectious relapses is a fair measure of what may be expected as to its effectiveness in preventing the latent manifestations of the disease.

Twenty-five years ago Ehrlich really paved the way for the use of arsenoxide when he maintained that the active spirochetocidal properties of "Ehrlich-Hata 606" (Salvarsan, Ehrlich's original) was due to oxidation. In 1920 Voegtlin and Smith found that oxidation was required before the trypanocidal effects of arsphenamine and neoarsphenamine were obtained. In 1932 Rosenthal demonstrated that no more than 10 to 12 per cent of arsphenamine is converted into arsenoxide within the body.

To be of definite value any new intravenous arsenical preparation must be known to be safe and to be of superior spirochetocidal value. Arsenoxide has long been ignored as being of possible usefulness because of its marked toxicity and potency. However, it is from the standpoint of comparison of the ratio of minimal curative to maximal tolerated dose that we should consider our drug. Should the ratio be higher for the more toxic one, we are forced to consider the more toxic one more favorably than the less toxic one. Regarding Mapharsen in this light Tatum and Cooper, who have studied the drug thoroughly, have concluded that it is a pure chemical substance not requiring biological assay as do the arsphenamines; that toxicity becomes slowly less marked on the oxidation of Mapharsen than the arsphenamines, which become fairly rapidly toxic; that the ratio of maximal tolerated to curative dose (therapeutic index) is greater for Mapharsen than neoarsphenamine in experimental animals; and, that the drug can be safely ampuled with sufficient sodium carbonate to neutralize the acid and sufficient sodium chloride to make an isotonic solution when the drug is dissolved in a stated amount of sterile distilled water preparatory to administration. The technic of neutralization of arsphenamine is more involved. It has also been shown that agitation and exposure to air are not productive of chemical changes or changes in toxicity.

Clinical reports have been encouraging. After giving 4,666 intravenous injections of Mapharsen in doses of 40 to 60 milligrams to 233 persons over a period of 18 months, Foerster and his associates concluded that "Mapharsen is a potent antisyphilitic agent and possesses special properties that justify an extensive study of this drug for a period years." One of the striking features of Mapharsen therapy has been the absence of reported nitritoid reactions. Other observers, such as Loveman, and Sullivan, have commented favorably after clinical trial on its low toxicity in therapeutic doses, the smaller therapeutic doses, adequate Wassermann reversals in early syphilis, and the prompt clearance of skin lesions. Sullivan remarked particularly on the gratifying results with Mapharsen in 4 cases of interstitial keratitis. Small dosage and low toxicity may prove it to be the intravenous drug of choice in the treatment of elderly patients with syphilis.

Moore and his associates at the Johns Hopkins Hospital Clinic studied the reversal of quantitatively titered Wassermann tests using Mapharsen, arsphenamine, silver arsphenamine, and bismuth arsphenamine sulphonate and found them to give approximately the same response. Neoarsphenamine was slightly less efficient.

Gruhzit and Dixon recently reported in the Archives of Dermatology and Syphilology a series of 75,589 injections over a period of almost 3 years in 4,841 cases of syphilis. They had the following comments to make:

> "Solutions of Mapharsen are easily made and are relatively stable. Exposure to air and agitation cause no change in its chemical nature or its toxicity. It possesses no danger of unexpected change in toxicity. Administration of solution of Mapharsen is simple. The average rate of injection of 10 to 20 seconds per dose of from 8 to 12 cc. appears optimum.
>
> "The average initial dose for adult patients of both sexes was 0.04 Gm. The subsequent maintenance dose for women was 0.04 Gm. Treatment consisted of weekly injections of Mapharsen for 8 weeks, followed by 8 weeks of treatment with heavy metal. The courses alternated

for 1 year or over without a rest period until 3 courses of Mapharsen and 3 courses of heavy metal were completed. A time treatment course of Mapharsen averaged between 0.98 and 1.38 Gm. of the drug. This amount of Mapharsen contains only about one tenth as much arsenic as a similar course of an arsphenamine.

"In a group of 4,841 patients, receiving 75,589 injections, no severe complications or death occurred. No instance of hemorrhagic encephalitis, hemolytic anemia, jaundice, severe exfoliative dermatitis, or severe nitritoid crises occurred. Moderately severe reactions necessitating discontinuation of treatment occurred 4.4 times per thousand injections. These reactions in preponderance were associated with gastro-intestinal disturbances.

"Spirochetes disappeared from moist lesions within from 24 to 48 hours after an initial dose of 0.04 Gm. Lesions healed more readily than similar syphilitic lesions under neoarsphenamine therapy.

"No patient with early syphilis was encountered whose condition did not respond to Mapharsen medication. In several instances early syphilis which did not respond to neoarsphenamine responded readily to Mapharsen therapy. Reversal of serologic reaction occurred under continuous treatment with Mapharsen for 1 year in 92 per cent of cases of secondary syphilis."

Miller and his associates at the University of California Medical School report a series of 13,240 injections given to 400 syphilitic patients over a period of almost 3 years. Their summary was as follows:

"In a clinical trial upon 400 cases of syphilis, it was found that Mapharsen: (1) Is safe to use, as shown by the 13,240 injections given to 400 patients. (2) Causes rapid healing of visible lesions. (3) Effects and maintains a Wassermann reversal within a reasonable length of time. (4) Is less toxic than neoarsphenamine. (5) Can generally be used where neoarsphenamine is not tolerated. Patients are thus able to continue with an arsenical in adequate dosage. This would not be possible if Mapharsen were not available. (6) Causes no nitritoid reactions. (7) Causes no Herxheimer reactions of consequence. (8) Causes no deaths."

The demonstration of the fact that Mapharsen can be used in patients sensitive to neoarsphenamine makes it a useful and worthwhile addition to our list of antisyphilitic drugs.

The results reported by Gruhzit and Dixon and by Miller and his associates are all favorable to the drug; they are a little glowing and tend to somewhat disprove my earlier statement that Mapharsen has not been definitely and finally established or proved as equal or superior to any or all of the intravenous arsenicals now accepted and used in the treatment of syphilis.

Kulchar and Barnett of San Francisco have recently reported in the American Journal of Syphilis, Gonorrhea and Venereal Diseases on their results with 1,270 injections of Mapharsen given to 56 patients with untreated primary or secondary syphilis during a period of 20 months. They found that pruritus, skin eruptions, and immediate reactions, including nitritoid crises, were slightly more frequent with neoarsphenamine than with Mapharsen, and that nausea, vomiting, diarrhea, and headache were more common with Mapharsen. Venous thromboses occurred following nearly 1 per cent of their injections of Mapharsen; none occurred with neoarsphenamine. They do not feel that serologic fastness and relapse, central nervous system involvement, and treatment reactions are avoided in early syphilis by the use of Mapharsen.

Cole of Cleveland, writing as a spokesman of the United States Pharmacopoeial Committee of Revision in the December 26, 1936, issue of the Journal of the American Medical Association, has the following comment to make with reference to Mapharsen:

"Another arsenical being employed quite extensively, and accepted by the Council on Pharmacy and Chemistry, is Mapharsen. It is administered by the intravenous route and is notable for the freedom from reactions, outside of gastro-intestinal reactions, following its use. It is employed in dosages of from 0.03 to 0.06 Gm., and the drug, after being dissolved in from 5 to 10 cc. of distilled water is administered rapidly intravenously. If the dose is given slowly, the patient may complain of pain up the arm. In this respect, rapidity of administration, it differs from arsphenamines. Mapharsen has now been used quite extensively and seems to have found a place in the therapy of syphilis. It may be used in place of arsphenamine or neoarsphenamine as the arsenical, especially if there is any reason why the others cannot be employed."

Mapharsen is ampuled by Parke, Davis & Co. in 20, 40, and 60 milligram ampules and larger clinic-size ampules of 0.5 gram. For purposes of administration the drug must be dissolved in sterile distilled water, and I have satisfactorily employed 5 cc. of water per 20 milligrams of the drug and injected the solution intravenously by syringe using a short bevel needle of 21 or 22 gauge, thus allowing about 20 to 30 seconds per injection. In my limited experience with the drug nausea and vomiting are the only reactions I have observed. The rapid rate of injection is utilized to prevent pain up the arm along the course of the vein at the time of administration and to minimize the possibility of the occurrence of venous thromboses. The maximum dose should not be administered to any patient at the first injection. An initial dose of 40 milligrams for men and 30 milligrams for women has been satisfactory. The second dose may be increased to 60 and 40 milligrams respectively. The usual maximum weekly dose may be regarded as 60 milligrams. For infants and children the initial dose should not exceed 0.5 milligram per kilogram of body weight. The total weekly dose for children is recommended as averaging between 0.5 and 1 milligram per kilogram of body weight.

I should call attention to the fact that in dissolving the powdered Mapharsen in water sufficient time should be allowed for the liberation of CO_2 before administration. Courses of treatment parallel the usual standard accepted routine for the other arsenicals.

Summary

A brief review of the experimental status of Mapharsen, a recent refinement in arsenical therapy, and abstracts from outstanding clinical reports have herewith been presented, including technic of administration, indications for its use and a discussion of its advantages and disadvantages as compared with the arsenicals now in accepted use.

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IDEAL VERSUS PRACTICAL TREATMENT OF EARLY NEUROSYPHILIS*

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The invasion of the nervous system by Spirochaeta pallida undoubtedly occurs very early in the syphilitic infection. This conception of the invasion of the central nervous system before involvement manifests itself in clinical changes was described first by Paul Ravaut in 1903. The transition from invasion to involvement occurs with the greatest frequency after the third year of the infection, the incidence increasing with the duration of the syphilitic process except in those cases in which the course of the disease is influenced by treatment. The stage of neurosyphilis recognized by abnormalities in the spinal fluid in the absence of subjective or other objective symptoms of central nervous system involvement is termed asymptomatic neurosyphilis. The frequency of this early invasion of the spinal fluid is variously reported. The actual incidence undoubtedly has not yet been reported, since there is not available a sufficiently large series of patients with untreated syphilis on whom routine spinal fluid examinations have been uniformly repeated during the early years of the infection. The frequency of the incidence of asymptomatic neurosyphilis in the series heretofore reported varies with the degree of selection of cases, the amount and character of the previous antisyphilitic treatment administered, and the duration of the infection. However, there is sufficient evidence available to indicate that every syphilitic should have a spinal-fluid examination made. Asymptomatic neurosyphilis is a highly important manifestation of syphilis because it may be the forerunner of clinical neurosyphilis. The early recognition and treatment of this type of neurosyphilis frequently prevents the development of the late clinical forms of neurosyphilis.

Prevention

The prevention of asymptomatic neurosyphilis is a possible accomplishment through the utilization of thorough treatment in early syphilis. The Coöperative Clinical Group has advocated for the early syphilitic patient a continuous scheme of treatment including at least 30 arsphenamine injections and an appropriate heavy metal administered in alternate courses (Table 1). In a group of patients so treated it was found that 80 per cent obtained a cure (Stokes, et al.). The spectacular achievements of early adequate treatment of syphilis under this uninterrupted schedule are familiar to every careful student. If it were possible to treat every patient with early syphilis so effectively, there would be little need of reporting the best methods of detecting and treating the late manifestations. Unfortunately, 60 to 80 per cent of those individuals who seek treatment for early syphilis lapse for long intervals or fail to continue treatment until they have received maximum benefit.

In addition to the half million individuals who seek treatment annually for syphilis in the early stage is a second half million who fail to seek any authorized medical care for syphilis and who are detected only when some late incapacitating condition brings them under observation. Evidence of the result of this neglect of treatment is demonstrated by a study of patients with paresis, tabes dorsalis and cardiovascular syphilis, from 50 to 70 per cent of whom had had no antisyphilitic treatment prior to the detection of these late manifestations.

Detection of Early Neurosyphilis

Since prevention of neurosyphilis is so handicapped by the lack of coöperation on the part of the patient with early syphilis, it becomes highly desirable to detect the involvement of the central nervous system as early as possible. There-

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TABLE 1

A SCHEME OF TREATMENT FOR EARLY SYPHILIS

DAY OR WEEK	ARSPHENAMINE	INTERIM TREATMENT	BLOOD WASSERMANN REACTION	REMARKS
day				
1	0.3–0.6	....	1	Arsphenamine dosage for first 3 injections at level of 0.1 gram for each 25 pounds body weight. Average subsequent dosage, 0.4 gram men; 0.3 gram women. In average patient all lesions heal rapidly and blood Wassermann reaction becomes negative during first course. If arsphenamine can not be used, substitute 8 to 10 doses 0.3 gram silver arsphenamine, or 10 to 12 maximum doses 0.9 gram neoarsphenamine. This applies also to subsequent courses.
5	0.3–0.6			
10	0.3–0.6			
week				
3	0.4			
4	0.4			
5	0.4			
6	0.4			
7	0.4	....	1	If mercury is used note overlap of 1 week at end of first and start of second arsphenamine courses. No overlaps necessary with bismuth. At this point a few days without treatment may be dangerous. Neurorecurrence.
8	....	Bismuth, 4 doses, 0.2 gram and K. I., or Ung. Hg. and K. I.		
9				
10				
11				
12	0.4	....	1	Arsphenamine starts, bismuth stops. Watch for provocative Wassermann reaction after first dose of arsphenamine.
13	0.4	....	1	
14	0.4	....	....	Try to prevent short lapses in treatment, especially at this early stage.
15	0.4			
16	0.4			
17	0.4	....	1	
18–23	....	Bismuth, 6 doses, or Ung. Hg. and K. I.	....	Bismuth is better than mercury. Use it if possible. Examine cerebrospinal fluid routinely at about this time.
24	0.4			
25	0.4			
26	0.4			
27	0.4			
28	0.4			
29	0.4			
30–37	....	Bismuth, 8 doses, or Hg. and K. I.	....	
38	0.4	....	1	
39	0.4			
40	0.4			
41	0.4			
42	0.4			
43	0.4	....	1	Patients with seronegative primary syphilis may cease treatment here, if blood Wassermann reaction has always been negative.
44–53	....	Bismuth, 10 doses, or Ung. Hg. and K. I.	....	Note that bismuth or mercury courses are gradually getting longer —4, 6, 8, and now 10 weeks.
54	0.4	....	1	
55	0.4	....	....	The average seropositive primary or early secondary patient should have at least 5 courses of arsphenamine.
56	0.4			
57	0.4			
58	0.4			
59	0.4	....	1	
60–69	....	Bismuth, 10 doses, or Ung. Hg. and K. I.	....	It is safer to finish treatment with bismuth or mercury rather than with arsphenamine.
70–122	(1)	No treatment	6–12	Blood Wassermann every month if possible; at least every other month.
123	Complete physical and neurologic examination, spinal puncture, and if possible, fluoroscopic examination of cardiovascular stripe.			
	Thereafter, yearly physical examinations, blood Wassermann every 6 to 12 months. If the two spinal fluid examinations above are negative, this need not be repeated.			

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[1] Probation.

fore, some definite recommendations as to the time and frequency with which the spinal fluid should be examined have been made by the Coöperative Clinical Group (O'Leary, et al.).

INDICATIONS FOR EXAMINATION OF SPINAL FLUID IN EARLY SYPHILIS

In patients with early syphilis the spinal fluid should be examined by the following rules:

1. Examinations should be made early in the course of and certainly before the completion of the sixth month of treatment. If the cell count is above normal and all other factors are normal, the test should be repeated at the completion of the course of treatment. If at the first examination of the spinal fluid the serum test is positive, subsequent tests should be made at intervals of 3 months to note the trend toward either the mild or the more severe (paretic) type of spinal fluid to be described later. If the first report is negative, subsequent reëxaminations may be required under certain conditions.
2. If the blood of a seropositive patient becomes negative during treatment and relapses to positive while treatment is continued, a test of the spinal fluid should be made.
3. If the patient neglects treatment and later returns for it, the spinal fluid should be examined even though the blood test has remained negative. Should the patient present symptoms of meningeal involvement, the spinal fluid must be tested.
4. The studies have clearly indicated that a patient with early syphilis who is treated properly and who at the sixth month of treatment is found to have a negative spinal fluid, may be assured that the spinal fluid will almost surely not become positive as long as the serologic blood reaction remains negative. As a final guaranty, however, the spinal fluid should be reëxamined at the completion of treatment.
5. Even though the blood becomes negative after treatment is started and remains so throughout the entire course of treatment, the spinal fluid should be examined before the patient is placed on observation or parole.

INDICATIONS FOR EXAMINATION OF SPINAL FLUID IN LATE SYPHILIS

In late syphilis the spinal fluid should be examined under the following conditions:

1. A test should be made early in the course of treatment. In the Coöperative Clinical Group studies it was found that if the disease is of 4 years or more duration, a negative reaction is evidence in more than 99 per cent of the cases in which patients have received treatment that the spinal fluid will not subsequently become positive. If, however, the spinal fluid is found to be positive, subsequent reëxaminations are necessary at intervals of 6 months. These repeated tests will show that the trend is toward a negative fluid, that the reactions are persistently the same, or that the fluid is progressing unfavorably toward the paretic type. This trend is indicative of the results which may be expected from treatment and may show the need for a change in the therapeutic regimen.
2. In a patient with late syphilis in whom the original examination of spinal fluid is negative a relapse in blood serology does not necessarily indicate that the spinal fluid has become involved. As has been pointed out, however, in early syphilis such a blood serologic relapse is of much more significance and another examination of the spinal fluid must be made at once. In a case of either early or late syphilis in which asymptomatic neurosyphilis has been demonstrated, a relapse in the serologic blood reaction from negative to positive warrants another examination of the spinal fluid.
3. In patients with asymptomatic neurosyphilis, repeated examinations of the spinal fluid are essential for the proper evaluation of treatment. Although both the blood and spinal fluid become negative, the spinal fluid should be reëxamined the first year and again the third year after the cessation of treatment.

SIGNIFICANCE OF THE SEVERAL SPINAL FLUID TESTS

The spinal fluid examination to be complete should include not only a complement fixation or flocculation test, but also an estimation of the globulin content, a cell count with cell differentiation, and a colloidal gold, benzoin or mastic test.

The characteristics of the spinal fluid are significant in patients with asymptomatic neurosyphilis. A classification of the degree of abnormalities of the spinal fluid into 4 groups permits more easily the determination of the ultimate prognosis and the modification of treatment in an effort to prevent the development of clinical neurosyphilis.

Typical spinal fluid abnormalities in individual patients with asymptomatic neurosyphilis are shown in Table 2.

Group I—mild. Cases in which the lymphocyte count is 10 to 20 cells, with or without a positive globulin test; the complement fixation or flocculation and colloidal tests are negative.

Group II—moderate. Cases in which the cell count and globulin content are normal or slightly increased; the complement fixation or flocculation test is positive, the colloidal tests are indeterminate or positive, and if the latter, are usually of the syphilitic zone type.

Group III—moderately severe. Cases in which the cell count is 30 or more, the complement fixation or flocculation test 4 plus, and the colloidal curve negative or of the syphilitic zone type. Patients falling just short of Group IV are also included in this group.

Group IV—severe. Cases in which the spinal fluid shows the so-called paretic formula, i.e., marked excess of globulin, strongly positive complement fixation or flocculation reactions (0.2 cc. or less of fluid), and the paretic type of colloidal curve. The cell count is above normal and contains, in addition to small lymphocytes, large lymphocytes and polymorphonuclear leukocytes.

INCIDENCE OF NEUROSYPHILIS

The Coöperative Clinical Group has studied 5,293 patients with syphilis who were under treatment or observation for 2 years or more and whose spinal fluid had been examined 1 or more times. The results of this study give relative frequency rather than actual incidence rates, because they represent individuals examined after varying amounts of therapy or under different treatment schedules, although to a large extent the tests were routinely given. The rates are reviewed here for their relative value (Table 3). Asymptomatic neurosyphilis is less frequent in the Negro than in the white race. Similarly, symptomatic neurosyphilis is more frequent in the white than in the colored race.

When the material studied was divided between those who began treatment in the early

TABLE 2

GENERAL CLASSIFICATION OF SPINAL FLUIDS BY DECREE OF ABNORMALITY FOUND ON EACH OF THE FOUR INDICATED EXAMINATIONS

GRADE	SEROLOGY	GLOBULIN	CELLS	COLLOIDAL BENZOIN OR GOLD
I	Negative	+ or −	10 to 20	000 000 333 000 000 0 0 0 3 3 3 3 0 0 0
II	2+ to 4+	+	8 to 10	000 000 333 000 000 0 0 0 3 3 3 0 0 0 0
III	3+ to 4+	+	30 to 100	021 221 333 310 000 0 1 2 5 5 5 3 0 0 0
IV	4+	+	30 to 100 10 to 30* 10 to 30**	333 333 321 000 000 5 5 5 5 5 4 3 2 1 0

* Large lymphocytes.

** Polymorphonuclear leukocytes.

TABLE 3

INCIDENCE OF NEUROSYPHILIS AMONG 5,293 PATIENTS BEGINNING TREATMENT IN THE EARLY AND IN THE LATE STAGES OF SYPHILIS, BY RACE AND SEX

	WHITE		COLORED	
	Male	Female	Male	Female
	per cent	*per cent*	*per cent*	*per cent*
Early syphilis:				
Asymptomatic	23.4	25.6	10.5	11.2
Symptomatic	13.9	10.7	11.1	5.9
Negative	62.8	63.7	78.4	82.9
	100.1	100.0	100.0	100.0
Late syphilis:				
Asymptomatic	11.9	12.3	8.3	7.5
Symptomatic	61.6	36.8	41.8	12.0
Negative	26.5	50.9	49.9	80.5
	100.0	100.0	100.0	100.0

stage of syphilis and those who neglected treatment until the late stage, the percentage of negative spinal fluids in the white male dropped from 63 to 27 per cent. Symptomatic neurosyphilis increased 2 to 5 times as the duration of the infection increased. Symptomatic neurosyphilis was manifest in more than half of the late cases of syphilis in which the spinal fluid was examined after the tenth year. As the duration of the disease increases, the frequency of asymptomatic neurosyphilis decreases while the symptomatic form increases (Fig. 1).

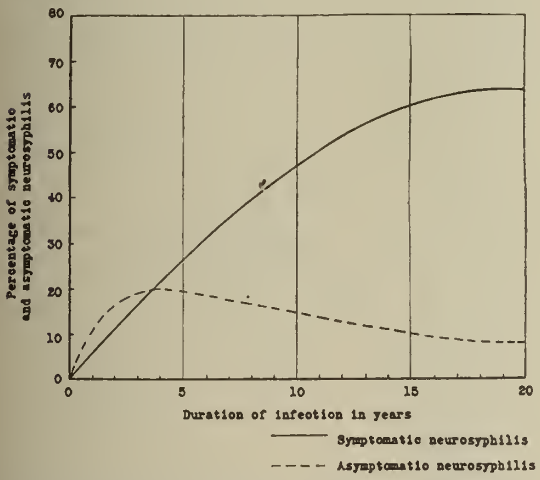

FIG. 1. Proportion of cases of syphilis with symptomatic or asymptomatic neurosyphilis, by duration of infection on detection of first abnormal spinal fluid.

NECESSITY FOR REGULARITY OF TREATMENT

Prolonged treatment of early syphilis loses much of its effectiveness in the prevention of neurosyphilis unless it is regularly administered. In Figure 2 is shown the result of haphazard treatment, despite the fact that as much treatment was given to one group of patients as to the other.

Since the majority of those infected with syphilis fail to avail themselves of ideal therapy it is essential that every physician recognize the dangers of irregular treatment. They may then warn their patients against further lapses and modify therapy accordingly.

SIGNIFICANCE OF SEROLOGIC BLOOD REACTIONS

Since the results of the serologic blood test are the most readily available to the physician treating syphilis it is highly desirable to determine their value as a guide. Undoubtedly the blood responds more readily to antisyphilitic treatment than does the spinal fluid. Therefore, a negative blood reaction is probably of less significance in evaluating the status of the spinal fluid in a treated than an untreated patient. In patients with early syphilis who received varying amounts of treatment the spinal fluid was positive in 31 per cent although the blood test was negative. Thus, a negative blood test in a treated patient frequently does not reveal the status of the spinal fluid.

In latent syphilitics who have received 20 or more injections of arsphenamine with appropriate heavy metals and the diagnosis is based on a negative spinal fluid and negative clinical examination, the chances are 99 out of 100 that the spinal fluid will remain negative despite the fact that the blood reaction may be persistently positive. The inability of the serologic blood test to reveal the presence of a positive spinal fluid in cases in which treatment has been given and the lack of significance of a positive blood test in a well-treated case of latent syphilis constitute two of the grave dangers of using the blood test alone as a guide in the diagnosis of central nervous system syphilis.

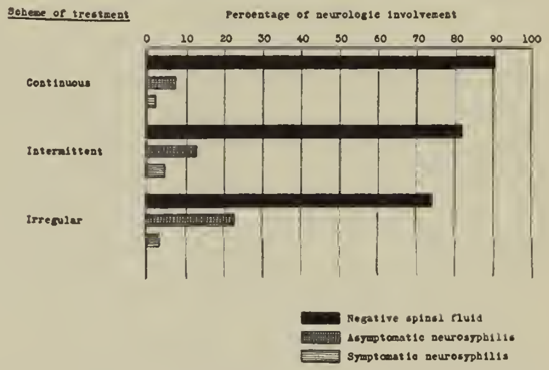

FIG. 2. Extent of neurologic involvement under specified treatment schemes in syphilitic patients adequately treated with arsphenamine and heavy metal previous to detection of neurosyphilis.

There are a number of cases in which the serologic blood reaction is a valuable guide to involvement of the spinal fluid. In patients with early syphilis who despite proper treatment have a persistently positive serologic blood test the chances are 3 to 1 that the patient has a positive spinal fluid. Blood serologic-fastness is more significant in early than in late syphilis. A fluctuating blood test in early syphilis though not as significant as the fixed one is also a guide. A study of such cases revealed that 29 per cent of the cases with a relapsed serologic blood reaction also had a relapse in the spinal fluid. Further, in those patients with early syphilis who previously had Group I or Group II types of spinal fluid with a relapse of the blood, the spinal fluid in 50 per cent of these cases became more strongly positive.

PRACTICAL TREATMENT OF EARLY NEUROSYPHILIS

By this time it is appreciated that the ideal treatment of early neurosyphilis consists of its prevention through the adequate treatment of the patient with early syphilis. From a practical standpoint, however, very few patients with early syphilis receive adequate treatment and it is improbable that all such patients will be properly treated in the near future. The clinical management of early neurosyphilis from a practical standpoint, therefore, is dependent upon recognition of this complication of syphilis at the earliest possible moment and the provision of suitable treatment for the patient sustaining such complications. The preceding facts which have been stated will assist materially in determining the seriousness of central nervous system involvement and aid the physician to a large extent in giving an accurate prognosis. Once these facts have been determined the next requirement is the judicious application of treatment along the following lines:

Figure 3 indicates the response of the 4 groups of spinal fluid to treatment. It will be seen that the less abnormal the spinal fluid the more readily it responds to treatment. Group I spinal fluids became normal in 84 per cent, Group II in 67 per cent, Group III in 62 per cent, and Group IV in 45 per cent. Figure 4 shows the percentage of clinical progression by the degree of abnormality in the spinal fluid.

Before adopting any scheme of treatment for early neurosyphilis it is necessary to obtain a knowledge of the patient's physical condition and to recognize complicating diseases. Use the least drastic therapeutic method first and under ordinary conditions continue with the original schedule until it has been proven inadequate by subsequent spinal fluid examinations.

In the patients studied with early or late asymptomatic neurosyphilis, 16 per cent had a Group I spinal fluid. Routine chemotherapy is usually successful in the treatment of the asymptomatic cases with this type of spinal fluid, and in the Coöperative Clinical Group material 69 per cent responded. However, it is essential to continue such treatment on the average for at least 6 to 12 months longer than in the uncomplicated case. The duration of the treatment should be controlled by means of spinal fluid examinations carried out at 6-month intervals, and treatment continued until the spinal fluid has been normal for 1 year. Of those patients whose spinal fluid failed to return to normal under routine chemotherapy, two thirds subsequently reversed after the application of other methods such as intraspinal therapy, tryparsamide, or malaria.

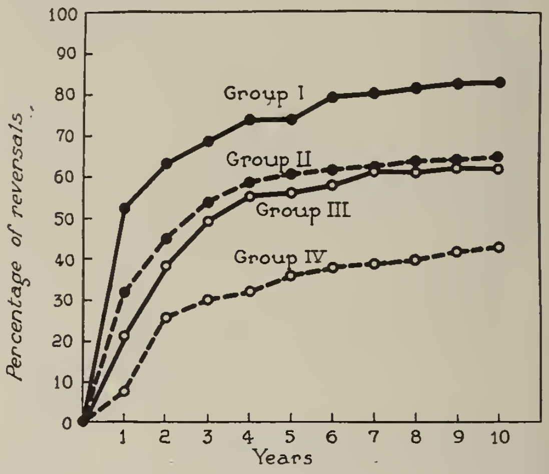

FIG. 3. Treatment reversals, according to spinal fluid grouping.

Patients with a Group II or III spinal fluid represented 65 per cent of the cases with early and late asymptomatic neurosyphilis. An intensified type of chemotherapy is advocated for these patients. This treatment should consist of relatively more arsphenamine and less heavy metal, more arsphenamine meaning larger doses, longer courses and a shorter interval between doses than is recommended in the standardized treatment for early syphilis. The interval between injections may be 4 or 5 days if the patient is tolerant, instead of a week. This plan of treatment must be continuous when applied to early neurosyphilis. Such intensified chemotherapy attained a reversal of the spinal fluid in 42 per cent of those with a Group II or Group III fluid. In 57 per cent of those who had failed to respond to routine therapy, the reaction was reversed under intraspinal, tryparsamide, or malaria therapy. The patients with asymptomatic neurosyphilis, Group IV spinal fluids, represented 19 per cent of the total. The intensified treatment with arsphenamine and heavy metal attained a serologic reversal in only 29 per cent of these patients. In such cases, because of the grave prognosis, the more drastic procedures are recommended without too much delay. Even treatment with tryparsamide, intraspinal or malaria therapy frequently is unsuccessful. Patients with this type fluid must be kept under careful and prolonged observation.

CONCLUSIONS

1. The ideal treatment of early neurosyphilis lies in its prevention through the utilization of adequate therapeutic methods in early syphilis; 80 per cent of adequately treated early syphilitic patients are cured and few ever sustain an involvement of the central nervous system.

2. From a practical standpoint few patients with early syphilis receive adequate treatment, and the problem becomes one of applying the most effective measures after early neurosyphilis develops.

3. Early diagnosis and an accurate determination of prognosis are factors of great importance in the clinical management of early neurosyphilis.

4. Indications are described for the examination of the spinal fluid in early and late syphilis.

5. A classification of the degrees of abnormality of the spinal fluid is made and its use permits an easier determination of prognosis when early neurosyphilis is present.

6. Studies of the incidence of neurosyphilis, including the present one, give the relative frequency of occurrence rather than actual incidence.

7. As the duration of syphilis increases, the frequency of asymptomatic neurosyphilis decreases while the symptomatic form increases.

8. Serologic tests of the blood respond more readily to antisyphilitic treatment than do serologic tests of the spinal fluid; a negative blood test in a treated patient frequently does not reveal the status of the spinal fluid.

9. A fluctuating serologic blood test in early syphilis may be indicative of a positive spinal fluid.

10. In latent syphilis, when the patient has a negative spinal fluid, the chances are 99 out of 100 that the spinal fluid will remain negative although the blood test may be persistently positive.

11. Systems of treatment are described for early neurosyphilis with various degrees of spinal fluid abnormality.

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SYPHILIS IN A MEDICAL CLINIC*

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Recently, among the medical profession, health departments, social agencies and the laity a lively interest has been manifested concerning the control of syphilis. The reason for this renewed activity can be traced to the far-seeing Surgeon General of the United States Public Health Service. In spite of the knowledge concerning syphilis, which is considered adequate for control, this disease is on the increase in this country.

I desire to present the problem of syphilis as found in a general medical clinic. The percentage of cases of syphilis found, although not specially sought, in a well organized general medical clinic is nothing less than sensational.

The most efficient medical clinics include routine blood serological tests for the detection o syphilis on all new patients admitted to the clinic, irrespective of their complaint. This practice has been followed at the George Washington University Hospital Clinic and Ward Service for 10 years. A study covering the last 9,179 admissions to the clinic was made. Syphilis was found to occur in 6.4 per cent of all admissions (Table 1).

TABLE 1

Cases of Syphilis among 9,179 Patients

	NUMBER
Primary Stage	30
Secondary Stage	306
Tertiary Stage	231
Congenital	20
Total	587 (6.4 per cent)

Incidence of Stages and Systemic Involvement

Among the 587 patients with syphilis, 30 were discovered in the primary stage, 19 of which were sero-positive. The genital organ of the male was the location for 23 of these chancres, 2 were on the lip of the female, 1 was on the lip of the male, 1 was on the breast of a female and the remaining 3 were on the genital organs of the female. In a venereal disease clinic this would seem a small percentage, but in a general medical clinic it is considered a high percentage. Every urogenital lesion is examined by the dark-field illumination one or more times. In some cases in which medication had been applied to the lesion, it required as many as 5 consecutive daily examinations of 1 sore before a diagnosis could be established. Between examinations the patient is instructed to soak the lesion in saline solution for 20 minutes every 3 hours. The smallest scratch and the most innocent appearing lesion very often will show the organism of syphilis from a careful dark-field scrutiny. The dark-field examination is of such paramount value in the detection of beginning syphilis, that we have established a permanent dark-field set up in a dark room, patterned after Stokes.

The policy of repeated blood serological tests and waiting for secondary lesions to appear, in the presence of a sore, before instituting treatment is to be condemned.

Varieties of chancre are described in text books, as painless, single sores of many characteristics; and while it is essential for the examiner to be familiar with all of these, the essence of success in detecting primary syphilis lies in repeated dark-field examinations of all suspicious extragenital lesions, as well as all urogenital lesions, suspicious or otherwise.

Ricord's classical observation, "Pas de chancre infectant sans bubon," is almost invariably correct. As a rule, one gland is markedly enlarged and is nearest the area of the initial lesion. The glands are not adherent to the skin and surrounding tissues and do not tend to suppurate. They are of india-rubber consistency and are not shotty as palpated in other types of infection.

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* Read before the joint meeting of the Social Hygiene Society and the Medical Society of the District of Columbia, March 17, 1937.

Among the 587 patients with syphilis, 306 were classified in the secondary stage. The early secondary cardinal symptoms and signs of syphilis are lesions on the body, sore throat, mucous-membrane patches and the loss of hair. These usually are the first signs seen in women. It is taught that syphilitic lesions do not itch and this is true in uncomplicated syphilis, but in many cases there are mixed infections which do cause itching. Time will not permit to describe these lesions, and they may be studied in any text-book on the subject.

In these 306 cases of secondary syphilis 43, or 14 per cent, were admitted to the clinic with a chief complaint of sore throat. The nose and throat specialists might discover syphilis in patients by use of the routine Wassermann test. In 2 of these 306 cases a mistaken diagnosis of neurodermatitis was made before the return of the routine blood serological report.

There were 124, or 21 per cent, of the syphilitics with gonorrhea or a history of gonorrhea. In every patient with gonorrhea a thorough, objective, impartial examination for syphilis should be made, including one or more blood serological tests (Creswell).

In this series there were 19, or 3.2 per cent, diabetics with syphilis. It is the consensus of opinion that there is no relation between the two diseases.

It is surprising from this study to observe that there were only 3 patients with syphilis and tuberculosis. As with diabetes and syphilis the general opinion exists that there is no relation between the two diseases.

There were 4 white and 5 colored women with the chief complaint of pregnancy found to have untreated syphilis. We agree with Moore, who says: "Since in the average pregnant woman, the most searching physical examination fails to reveal any evidence of the existence of syphilitic infection, the best and usually only way to recognize its presence is by means of the routine use of the blood Wassermann."

In this series of 587 cases of syphilis, 231 were of the tertiary variety. The secondary and tertiary stages of syphilis often overlap and merge, and we made the division arbitrarily from clinical findings. Tertiary lesions are degenerative and the secondary lesions are irritative. For the sake of simplicity in this study we have included cardiovascular syphilis and neurosyphilis in the tertiary group (Tables 2 and 3). Cardiovascular syphilis in a medical clinic is common. In this series 97 syphilitic patients had cardiovascular involvement (Table 2). Of these, 71 were of the simple aortitis variety, which is most amenable to treatment. Patients over 35 years of age, with a positive blood test for syphilis, without clinical manifestations, should have an X-ray examination for the detection of early cardiovascular disease. In this way many cases will be discovered before definite clinical signs appear.

TABLE 2

Incidence and Kinds of Cardiovascular Syphilis among 587 Cases

	NUMBER	PER CENT
Aortitis (simple)	71	73
Aortic insufficiency	12	12.5
Aneurism	14	14.5
Total	97	16.5

Forty-three, or 7.3 per cent, of the cases had neurosyphilis (Table 3). Of these, 19 were asymptomatic, a fact which demonstrates the value of the routine examination of the spinal fluid in all cases of syphilis. All latent syphilitics should have the spinal-fluid examination at once, and should it be negative, it is certain that it will remain so. In early syphilis, the time for the spinal-fluid examination is at about the sixth month of treatment. Changes occur in the spinal fluid many months and often years before subjective symptoms and objective signs appear

TABLE 3

Incidence of Asymptomatic and Advanced Neurosyphilis among 587 Cases

	NUMBER
Asymptomatic	19
Advanced (clinical signs)	24
Total	43 (7.3 per cent)

that can be detected by neurological examination.

One of the surgical staff enucleated a "skin tumor" from the shoulder of a patient. The pathologist reported from microscopic examination of a section of tumor, a marked perivascular, round-cell infiltration, indicating that syphilis should be excluded. Final diagnosis was made of gumma. The same thing occurred in another case, in which the lesion was situated on the tongue. This is no reflection on the surgeon, except that he, as well as each of us should think of syphilis when examining lesions.

It is generally conceded that syphilis is more prevalent in the colored race than in the white race. In our clinic we found syphilis slightly more common in colored females than in colored males, but the opposite in the white race (Table 4).

TABLE 4

Incidence of Syphilis according to Sex and Color among 587 Cases

	NUMBER
White Male	131
White Female	128
Colored Male	144
Colored Female	184

Diagnosis of Syphilis

The diagnosis of syphilis in any stage is difficult, but with care and thought a diagnostic impression often can be formulated even before serologic results are reported. Table 5 shows a rather high diagnostic impression of syphilis made by the medical men prior to blood reports.

TABLE 5

	NUMBER	PER CENT
Diagnosis made or diagnostic impression formed of syphilis prior to blood test or dark-field illumination	289	48.9
Positive routine blood test. No detectable symptoms or signs	298	51.1

Since the diagnoses of syphilis in over one half depends on the blood serological reaction, one who deals with this disease should have a thorough knowledge of the technic, value and shortcomings of serologic tests. The Wassermann and Kahn tests are employed routinely in this clinic, and all blood sera and spinal fluid are titered. Dr. E. B. Vedder, Head of the Department of Experimental Medicine, conducts the tests in the following manner. The titration for spinal fluids is performed by setting up a series of tubes containing 1.0, 0.5, 0.4, 0.3, 0.2, 0.1 cc. of spinal fluid. With blood serum each successive tube contains one half the former, i.e., 0.1, 0.05, 0.025, 0.012, 0.006, 0.003 cc. of serum. For such titrations the Wassermann test lends itself with more ease and flexibility than the Kahn test.

Such titrations of all spinal fluids and of the blood sera in all positive cases is of great value as a guide to treatment. Nothing is more annoying, especially to the patient, than to treat a case energetically and to hopefully send in the blood, only to find that the reaction is still 4 plus. When the serum is titrated, the exact strength of the reaction is known in advance, and may be seen to clear up gradually as the result of treatment. It is also clear that when blood reactions are 4 plus with very minute amounts of serum, such as 0.025 to 0.003 cc. very intensive treatment will be required to render such a reaction negative in the amount usually used (0.1 cc.).

Such titration is also of some diagnostic significance, since the positive reaction obtained in a series of tubes with diminishing amounts of serum cannot be casually dismissed as a possible error in technic or as a reaction of no clinical significance in cases having no symptoms of syphilis. Even in cases in which the diagnosis is obviously some other disease, a very strong Wassermann or Kahn test indicates concomitant latent syphilis as a complication, and the treatment of the latter will very possibly influence the former favorably.

All serologists have noted increased speed of hemolysis and decreased sensitivity, or decreased speed of hemolysis and increased sensitivity in tests made on different days, and these varying speeds of reaction are the main cause of daily variations in the strength of the Wassermann reaction. The most common cause of these fluctuations is the use of an excessive or deficient amount of complement indicated by the preliminary titration. For example, if the preliminary titration results in complete hemolysis with 0.05 cc. of complement, 0.1 cc. will be used in the final tests, and this is the optimum amount. Should the preliminary titration indicate a complement requiring 0.07 cc. to produce complete hemolysis and this is doubled, 0.14 cc. would be used in the final tests, which would then be too rapid and cause loss of sensitivity. This can be compensated for by using an amount of complement in the final tests somewhat less than double the amount as determined by the titration (in this case, 0.12 cc.). On the other hand, when the titration is low, (0.03 to 0.04 cc.) somewhat more than twice the amount should be used. That is, an approximation is made toward the normal amount used in the tests, which is 0.1 cc. The competent serologist can therefore eliminate these daily fluctuations, both by better judgment in the use of complement and in reading the completed tests. The results of the Wassermann test have never been so good since this test has been left in the hands of technicians, and this is a main reason for the superiority of the Kahn test in the hands of the average technician. The Wassermann reaction should always be controlled, and the results read by a trained serologist.

Other factors cause variations in the strength of the reaction more rarely. These include the ingestion of alcohol, which reduces the strength of the reaction, and bacteria growing in the blood serum when kept too long, even in the usual ice box.

Treatment of Syphilis

In dealing with the patient with syphilis an attempt should be made to dispel the belief still held by many in the case of venereal disease that the punishment fits the crime. On the other hand, so little is thought of venereal disease by many people, that they look upon it as no worse than a bad cold.

To secure coöperation and results from an examination and treatment a friendly manner with the patient is necessary, the physician bearing in mind the old maxim, "A faithful friend is the medicine of life." He should speak the vernacular and be persistent though tactful; if there are findings present they most certainly will be elicited. It has been said that "A smile in a clinic is worth 2 follow-up workers."

According to our records 313, or 53.3 per cent (Table 6), of the 587 patients with syphilis had not received any antisyphilitic treatment. Since a large number of these were apparently surprised and shocked when informed of their disease, some may have sought treatment elsewhere.

TABLE 6

Incidence of Treatment among 587 Patients

	NUMBER	PER CENT
Patients with no treatment	313	53.3
Referred to other clinics	139	23.6
Patients who started treatment and discontinued without advice	169	28.8
Patients with satisfactory treatment	76	12.9

Others who had not sought treatment were probably better off than the 169, or 28.8 per cent, who received a few injections and discontinued them without advice. On this point of inadequate treatment, Chesney says: "A small amount of treatment in early syphilis is worse than none, precisely because it interferes with the body's own defensive mechanism, while at the same time it often fails to eliminate the infection. It leaves the patient worse off than nature alone would have left him, and is, therefore, greatly to be condemned."

Patients who were unable to pay the small fee required by the clinic for antisyphilitic therapy numbered 139, or 23.6 per cent. These patients were handed a written report of their examination and referred to the city free clinics for treatment.

Of the 587 cases of syphilis, 76, or 12.9 per cent, received satisfactory treatment. By this is meant that they completed the full prescribed courses of uninterrupted antisyphilitic therapy. In addition, a thorough examination for complications was made before releasing the patient for the rest interval.

Social Service Follow-up of Syphilitic Patients

The only form of social-service contact of syphilis cases in this clinic is by follow-up letter. There is no field social-service worker who should be a permanent part of every clinic. From 343 letters sent to patients delinquent in receiving treatment, answers were received from 27, or 7.9 per cent. Many letters were returned because of incorrect address, and others were ignored.

The remedy for such a condition can be attained only by the authorities providing adequate physical equipment and furnishing trained workers for follow-up of cases, tracing contacts and keeping delinquent patients in regular attendance for treatment.

While the syphilis problem encountered in this medical clinic is in no way a cross-section of the country's problem of the disease, or of syphilis clinics, it reflects well the story of the average clinic-syphilitic whose control is an urgent need and an important cog in the larger problem.

A coöperative program, as yet not adequately formulated, to include local health departments and private physicians is urged.

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WHAT THE HEALTH DEPARTMENT IS DOING IN THE PREVENTION AND TREATMENT OF THE VENEREAL DISEASES*

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Washington

The venereal diseases have long been known to be communicable diseases, and the prevention of the spread of these diseases under the law has become a responsibility of the various health departments. A brief survey of what the Health Department of the District of Columbia is doing in this matter may be of interest.

Since early in the 1880's one of the important functions of the Health Department Laboratory was to aid the physician in the examination of smears for gonorrhea. Since 1911, soon after the Wassermann technic was discovered, it has lent its aid through dark-field examinations and blood tests to the diagnosis of syphilis. This work of the laboratory, of course, has increased immensely as the years have gone by. The following tabulation shows this increase during the past 5 years:

YEAR	BLOOD TESTS	PER CENT POSITIVE	GONORRHEA SMEARS	PER CENT POSITIVE
1936	23,624	27.2	11,478	50.9
1935	21,458	28.3	9,789	52.7
1934	17,351	30.7	8,736	50.6
1933	15,966	30.0	6,090	41.3
1932	14,386	25.3	5,537	39.9

This is an increase of 64 per cent in the number of blood tests and 107 per cent in gonorrheal smears during this 5-year period. The Wassermann reaction is used as the routine test, and the Kahn test is used only when the Wassermann is partially positive, as a further check. The dark-field examinations are made at the Social Hygiene Clinic.

It is the fixed policy of the laboratory to examine all specimens submitted to it, regardless of the financial status of the patient, that being left to the discrimination of his physician. This policy is applicable in all laboratory examinations for communicable diseases.

In 1918, through a special appropriation of Congress, a clinic was established for the cure and prevention of the venereal diseases. This clinic was given the name of the Social Hygiene Clinic. It was established for the care of the indigent only, and this policy has been adhered to closely up to the present time. The work of this clinic, of course, has increased greatly since that time. The following figures show the increase since 1922:

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* Read before the Annual Scientific Assembly of the Society, May 5, 1937.

YEAR	CLINIC ATTENDANCE
1922	11,898
1927	18,438
1932	39,198
1933	50,795
1934	56,184
1935	68,094
1936	76,592

The clinic attendance had doubled about every 5 years. It has been necessary to increase the clinic hours during the past year. The personnel has been increased from time to time. At present there are 8 part-time physicians, 5 nurses, and 2 social-service workers.

The distribution of patients according to race and sex is shown by the following figures:

	per cent
White:	
Male	17
Female	8
Total	25
Colored:	
Male	47
Female	28
Total	75
Total males	64
Total females	36

Thus the colored outnumber the white 3 to 1, while the males in both races outnumber the females almost 2 to 1, although the females seem to be a little more faithful in keeping up treatment.

The marital status of the patients is as follows:

STATUS	PER CENT
Married	30
Single	60
Widowed or separated	10

These figures are probably quite misleading, since many who are married do not admit it, and many admitting marriage are living apart.

The next figures show the diagnosis of the 6,171 new cases examined last year:

DISEASE	NUMBER OF PATIENTS	PER CENT
Gonorrhea	1,186	19.2
Syphilis	1,889	30.6
Chancroid	36	0.6
No venereal disease	3,060	49.6
Total	6,171	

The large percentage of noninfected cases is due, no doubt, to the large number of persons sent in for examination by the courts and other agencies and also of those examined as suspected contacts. Both gonorrhea and syphilis were found in 14 per cent of such cases, often when there were symptoms of only one disease.

It has been noted that the more convenient the clinic is to the patient, the more regularly he will attend. Many come naturally from the poorer sections of the city, where housing conditions are bad. Many of these patients are out of work or on relief. The control of the venereal diseases is, of course, not only a social problem but also an economic problem.

A very large majority of the patients (82 per cent) were between the ages of 15 and 40, as shown by the following figures:

Under 5 years	21
5 to 15 years	379
15 to 25 years	2,830
25 to 40 years	2,237
Over 40 years	704
Total	6,171

A survey of a recent month's records shows the sources from which the patients are referred to the clinic:

Friends or old patients	153
Relatives	107
Employers	23
Physicians	47
Hospitals or clinics	94
Central Admitting Bureau	19
Relief Agencies	58
Courts	28
Newspaper articles	23
Other	26
Total	578

The next figures show by whom the diseases are spread:

Prostitutes	36
Clandestine prostitutes	57
Mutual friend	132
Marital partner	127
No recent exposure	109
Unknown or denied	117
Total	578

The diagnosis is made according to scientific standards—gonorrhea by smears, syphilis by dark-field examination and blood tests, repeated if necessary. X-ray examinations and spinal fluid tests are recommended in many instances.

The treatment of each disease is carried out according to accepted standards. For syphilis the old arsphenamine is used in preference to the new. It is the present policy to treat these diseases in all stages, regardless of contagiousness. This is considered best for the patient and the public tax-payer. The patient is supplied with pamphlets describing his disease and what is expected of him. Definite written instructions in regard to home treatment are given to him. He is strongly urged to take regular treatment. Our delinquency is appalling, but we hope this may be improved with a better follow-up service.

In conjunction with the Medical Society of the District of Columbia and the Social Hygiene Society, the Health Department has taken an active part in the recent venereal disease campaign. It is felt that by making the public better acquainted with these diseases, more people will seek treatment early and thus protect others.

What is the physician's part in this program? Coöperation with the Health Department will help him in many ways. In 1927 a law was passed in the District of Columbia requiring the physician to report all venereal diseases to the Health Officer. This may be done by number. If the patient is delinquent and a danger to others, the physician should then report him to the Health Officer by name and address. It is then his duty to see that he is treated until well. In the near future a method by which the physician can do this with a minimal amount of trouble and no expense will be inaugurated. Thus the physician can use the Health Department not only as an aid in diagnosis, but as a means of preventing the spread of these diseases. A large percentage of all venereal cases goes to the private physician first. Consequently he is the vital factor in the control of these diseases. It is urged that the venereal disease committee of this Society confer repeatedly with the Health Officer as to any future policy.

In conclusion, it may be stressed that the control of these diseases can be successful only with the whole-hearted coöperation of the medical profession. Physicians constitute the shock troops in the battle against the venereal diseases, more valuable than all of the many clinics and hospitals, voluntary and official. The success of any venereal disease program will depend on the coöperation and efforts of the physicians treating these diseases.

Myelomalacia Following Spinal Anesthesia.—The patient was a man, aged 33, a pastrycook. Apart from bronchitis during the previous 3 years his general health had been good. He was admitted to hospital on account of a displaced right semilunar cartilage and on September 3, 1934, this was operated on under a spinal anesthetic. The anesthetic used was spinocaine, of which 2 cc. were injected after lumbar puncture between the third and fourth lumbar vertebrae. He had no symptoms until a week after the operation, when he complained of pain in the lumbosacral region of the spine. He made a good recovery from the operation, however, and was discharged from hospital, walking, on September 15. Toward the end of September, nearly a month after the operation, he began to have pain in the left knee and increasing difficulty in walking. He had to go to bed, and a feeling of numbness developed in the left foot and gradually spread up the leg. At the same time the right leg became weak and the pain in the back increased, so that he had difficulty in turning in bed. This pain spread upwards and became severe and gripping around the waist. He was readmitted to hospital on October 24 and on that date developed retention of urine. . . . There was marked weakness of flexion of the spine on the hips and the patient was unable to sit up unaided. The abdominal reflexes were absent. In the lower limbs there was moderate wasting of all muscles which was least marked in the hamstrings and most marked in the peronei and anterior tibial group and was symmetrical. There was bilateral foot-drop and almost complete flaccid palsy of both lower limbs except for an extremely feeble movement of flexion and extension of the right hip. The knee and ankle-jerks were absent and the plantar responses were a very feeble flexor. There was slight impairment of appreciation of light touch over the dorsum of both feet and considerable loss of sensibility to pin-prick over all the sacral-segmental areas. There was gross loss of postural sensibility in the toes of both feet and the vibration of a tuning fork was not appreciated over the feet or the left shin but was felt over the right shin. There was retention of urine and obstinate constipation. Lumbar puncture on October 30 yielded the following results: Protein 0.270 per cent, globulin ++, no excess of cells, Wassermann reaction negative. Subsequently there was no change in the patient's neurological condition and he died on December 24, 1934, from complicating infection. Pathological examination, ... showed a massive softening of the spinal cord, maximal at the level of the upper part of the lumbar enlargement. . . .

Discussion on the Neurological Sequelae of Spinal Anesthesia. RUSSELL BRAIN, M.D., and DOROTHY RUSSELL, M.D., *Proceedings of the Royal Society of Medicine, June, 1937, p. 1,024.*

WILLIAM ALANSON WHITE, M.D., M.A., D.Sc., LL.D. HIS INFLUENCE ON THE MEDICAL PROFESSION*

William J. Mallory
Washington

> "Evolution . . . is a movement in thought, not the swing of an axe. . . . The true servants of this mysterious movement . . . are the inspired talkers who sit peacefully at meat with their fellow-men."

William Alanson White came to Washington in 1903 as Superintendent of Saint Elizabeth's Hospital. He was then 33 years of age and from that time until his death, March 7, 1937, that is, for more than a third of a century, he conducted the affairs of this great institution, ministering to the care and treatment of between five and six thousand patients and affording training for a large medical staff, nurses and attendants.

If he had done nothing more than organize, develop and govern Saint Elizabeth's Hospital he still would have accomplished a notable work.

The situation of the old administration building on Congress Heights, looking down on Washington and the nearby waterways suggests a light-house, but in the realm of ideas he was more than the keeper of a light-house because he became an organizer, explorer and colonizer.

He organized and developed his hospital so that Kraepelin, "the Father of Psychiatry" described it as the first in every respect.

As one of the explorers of the darker continents of thought, he knew the jungle ways of emotion, and wherever his spoken or written word reached he planted some original ideas and showed new pathways of approaching old problems.

What his life and work meant and still mean to the medical profession of the city of Washington can be evaluated better by recalling some of the points of contact that he developed and the channels of communication that he created in his intercourse with people and institutions here.

From 1906, when he became a member of the Medical Society of the District of Columbia by invitation, his influence was increasingly felt, and his fellowship more and more highly valued. He was considered "one of us" by every one of the organizations of which he was a member.

His many papers, contributed to the scientific programs, although dealing as a rule with some aspect of psychiatry, a specialty of which the general practitioner is somewhat shy, evoked the interest of other specialists as well as general practitioners, held their attention to the subject and enlivened the new lines of thought in relation to each man's particular field of work

At the many medico-social affairs of Washington, such as banquets, smokers, class meetings and gatherings of student fraternities, his evident enjoyment was so contagious that every one shared it, and he was therefore much sought after both as guest and speaker.

However, he manifested an almost Paulist missionary zeal, for while he would often begin a talk by pleasantly twitting and teasing the toastmaster or other speakers on some vulnerable point, the occasion was always used appropriately for saying something that was both interesting and worth remembering.

Proceeding from allusion or apt quotation, he would elaborate some novel point of view, or illustrate the application of some fact or principle of other branches of science to the understanding and treatment of the patient.

It was, therefore, only natural that he should be a member of many organizations, but he seemed to have a definite preference for those pertaining to public health, social hygiene, and, more especially, mental hygiene and education in its broadest sense. For these he seemed to reserve his greatest talent and best effort.

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* Read before the Academy of Medicine of Washington, D. C., May 18, 1937.

When elected to office he was no mere title holder, but, as in the case of the Social Hygiene Society, he became a vigorous leader and wise director, galvanizing the organization into new life and purpose.

If appropriate social instrumentality did not exist he proceeded, with the aid of other enthusiasts in the cause, to create one, as he did when he founded and became the first president of the Washington Institute of Mental Hygiene. Prior to this there was no place where people who were unable to pay for it, could obtain neuropsychiatric advice or guidance, until they became so deeply involved through mental illness or maladjustment that admission or legal commitment to a public institution became necessary.

From 1904 until his death he taught psychiatry in the United States Army and Navy Medical School and gave clinical courses at Saint Elizabeth's Hospital for the Medical Corps of these services. He is credited with having introduced psychiatry into the military service.

At the close of the World War, when the United States Veterans' Administration was confronted by the gigantic problem of thousands of soldiers in need of neuropsychiatric examinations, classification and treatment with no sufficient personnel available, he organized at Saint Elizabeth's Hospital a postgraduate school. He brought there eminent teachers and clinicians, mobilized his own staff, and devoted his unstinted personal services to the training of men to meet this new and urgent need.

Many of the doctors who passed through this school and those who served on his staff are now occupying posts of importance and responsibility in the public services, teaching institutions and private practice.

As a member of the faculty of the George Washington University School of Medicine he took a helpful interest in not only the teaching of psychiatry, but also the wider problem of organization and teacher-student relations. He faithfully attended faculty and committee meetings and personally participated in examinations.

In faculty discussions of delinquent or conditioned students his inquiries were incisive concerning the reason for the falling off in early promising scholarship, and his interest seemed to be more in understanding and improving unfavorable conditions than in the formulation and application of rules.

In educational councils he advocated an important place for psychiatry in the curriculum.

During the time when specialization was developing to an extreme degree, both in thought and practice, his influence on the philosophy of medicine was that of an integrator. He endeavored to synthesize the various branches of medicine around the concept "The organism functions as a whole." "All reactions are total reactions."

His assumption was that the psyche is as old as the soma; both have their paleontology, embryology, vestigial structures, comparative anatomy and physiology.

He said: "Mental reactions as we know them have a historical development as old as the bodily reactions and, like them, can only be adequately understood in the light of their historical backgrounds. If then the psyche has a historical background equal in duration to that of the soma, it follows again on the principle of logical fate that it must have its embryology, its comparative anatomy and its paleontology, and this is, of course, true."

He set a fine example to the members of the profession concerning education of the public in medical matters. He wrote and spoke on psychiatric and allied subjects in a manner which, while clear and interesting, was to all classes of physicians, lawyers and laymen entirely devoid of sensationalism and emotional features or any trace of self-aggrandizement.

His ideas stimulated thought and discussion. In speaking and writing he assumed the points of view and methods of elucidation that in the opinion of some of his colleagues were novel and progressive to the point of radicalism, but in practice he was a conservative physiological therapist.

Advocates of sterlization or of "mercy deaths" left him cold; and loving relatives who would rather see their dear ones die—of an experiment—than live in a distressing condition, could not move him from the attitude that when a patient came under his care no one and nothing could relieve him of responsible custodianship of the life, health and welfare of that patient.

Although he was a great specialist and helped to make psychiatry a greater specialty than it ever was before, he accomplished this not by magnifying psychiatry as such but by developing the idea that "psychiatry no longer preoccupies itself with the so-called insane. Subtle distortions of personality have come to be recognized as perhaps even more significant in determining a course of events in our complex civilization than are the troublesome maladjustments or disabling psychoses."

The common situations faced by every one, such as organic disease, physical trauma or surgical operation, may be the important factor in precipitating such "subtle disturbances of the personality or disabling psychoses." He held that some appreciation of these relations should be expected of every doctor of medicine.

His profound interest in the formation of this new society, the Academy of Medicine, was due to the hope and expectation, that in this body of men, representing so many branches of science, there would develop an appreciative sense of the interrelation and even the identity of the sciences, and that a unity of purpose in their application to the promotion of the welfare of man would follow.

He hoped that the clinician might become better acquainted with the factual material and precise methods of science, and that the pure scientist might learn something more of the requirements and limitations under which knowledge must be applied in the promotion of mental and physical health.

His sympathy was broad, deep and intense, but did not manifest itself as an emotional state. He ever translated this into action; by teaching and in consultations he advocated the idea that the hysterical was not a culprit, nor the pervert a criminal, but that they were examples of normal impulse frustrated, or biological energy arrested at a primitive level, and that therapeutic measures should not be aimed at further suppression or punishment, but toward release and redirection of this energy into socially useful channels.

All sorts and conditions of men, women and children wrote to him, seeking his aid and guidance, and he replied to child, hobo, and minister of state, with the same care, and the same delicate touch of personal interest and conversational tone.

His influence on young men was wholesome and helpful. Some one has written: "Over and above all the help we can get from our ordinary training, association with our betters, and a very limited experience, we can pick up from literature a few fundamental ideas as to how the great game of life has been played by the best players."

Dr. White was certainly one of the best players of The Great Game. His technic was such that his many honors aroused no jealousy, and his deserved eminence provoked no envy, but rather emulation.

In addition to offices too numerous to mention here, he enjoyed, while still alive, the distinction of having a society named in his honor, The William Alanson White Psychiatric Society, and the tribute of having a foundation endowed in his name—The William Alanson White Psychoanalytic Foundation.

His last public appearance was at a testimonial dinner given to one of his former interns, later for many years a member of the Board of Visitors of Saint Elizabeth's Hospital. He was to have spoken of the close relation which existed between primitive medicine and religion, their later divergence of interest, and their more recent coördination of function in social service. He had already written elsewhere:

"My own feeling is that tolerance is the basis upon which the structure of human thinking can be erected, that will make for such a mutual appreciation and understanding as will cement human relationships in a way consonant with the further progress in culture that is our main social objective."

Dr. White left to all who knew him the happy memory of his humane character, and the inspiration of his life work. He left upon a great institution, Saint Elizabeth's Hospital, a guiding impetus which will long be effective. Under his influence this hospital became a model institution and social agency.

While providing care for the sick, he developed it into an educational institution where many sick were rehabilitated; nurses and doctors were trained; scientific observations were made; material, from history sheet to pathologic laboratory, was collected; information published; and capable, well-trained men and women sent out into the wider world to work.

To the medical profession, so frequently discouraged, by human misery, morbidity and mortality, he left a hopeful practical philosophy. Neither heredity nor determinism were stumbling blocks to him, for he wrote:

"We know that if we act 'as if' we could modify human beings, 'as if' their difficulties were removable, 'as if' they could be cured—so to speak, of certain disabilities, it is truly remarkable what extraordinary results are sometimes obtained, so that both in the field of determinism and in that of heredity we must pursue a philosophy of 'as if.' "

If the old folk ways and *mores* seemed out of harmony with changing conditions and hindered progress, he did not try to discredit the past, or destroy a vestigial structure of the mind, or the body, or society, but he did labor to give such things a new and true interpretation which would enable modern man in rapidly changing circumstances to utilize effectively these old agencies with all the driving power of their emotional content.

He wrote: ". . . for evolution, for progress, for development, and for better conditions of living, in order that we may the more intelligently go forward with the times in a feeling of sympathetic coöperation, with that underlying hope in their aspirational value that we have always felt somehow controlled the order of things."

And again: "It would seem that social organization was tending in the direction of increased individual freedom, retaining and building up only such institutions as minister to the end of personal freedom by creating a millieu in which it can be safely exercised and brought to its fullest possible fruition."

Some of his sentences take on weighty significance at the present time. For example, "Peace, industrialism, and a reasonably stable structure built upon principles of law and order, specialized classes for producing necessities, for defense, and for policing, are necessary, that activity represented by science and art may develop."

"Now, if any of this group should come to dominate the activities of the whole social organism, it would be sick. Society needs all their activities, but it needs them as the body needs its organs, subordinated to the needs of the whole."

Like other thoughtful men of experience, he did not seem to think that the consumption of goods would bring contentment or culture, for he wrote:

"Peace resides within. It is not dependent upon things without. It is the inner values that count most, and it is to their cultivation that civilization should turn."

His full life, devoted industriously and intelligently to hard work, would lead one to believe that he agreed with Paderewski, who wrote: "Creative work, take it as you will, is the only thing in life that gives supreme satisfaction. Ideas are eternal. In presenting them you reach the heights. The form of presentation makes no difference. By creative work you are giving yourself new life. Creative work kills death."

Dr. White left no children of his body, but every man who attended his lectures and clinics or read his many essays and books would be quick to admit that there was some fine part of his own intellectual personality to which William A. White was truly sire.

His voluminous works, from formal textbooks to semi-popular essays, are premeated with the idea of intelligent intervention in the distressing confusion of human relationships.

I should like to see in the archives of this Academy a complete file of his text-books, essays and papers, marked with a tablet bearing the lines of A. E. Housman's dedicatory verse to his volume of posthumous poems:

> "Here's to all mistreated fellows,
>   Unborn and unbegot,
> For them to read when they're in trouble,
>   And I am not."

ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"THE RELATIONSHIP OF FEAR TO THE GENERAL CONDITION OF THE SURGICAL PATIENT,"* **Norman E. Freeman, M.D.**, Philadelphia.

Fear has been defined as the exaggeration of that alertness to the presence of danger which is such a valuable defensive mechanism. As Cannon has pointed out, the physiological reactions to fear equip the organism for vigorous physical activity. Under present conditions of civilization, the response to fear does not necessarily involve action. The bodily mechanisms persist although the need for them is past.

It is recognized that many specific disease processes may originate or be exaggerated by fear. When the disease is clearly organic, does fear play a rôle which may determine the outcome? The emotional attitude of the patient is a factor which may affect the success or failure of a surgical procedure. Since the patient's ability to stand an operation depends upon his so-called "general condition," the effect of fear on physiological processes was studied.

In surgical shock, the blood volume is reduced. Previous studies on the mechanism of reduction of blood volume indicated that the loss probably occurred through stasis of blood in the vessels. Observations were, therefore, made on the volume flow of blood through the hand in patients in an attempt to discover what factors produced the stasis.

In the normal individual, the blood flow through the hand was found to be sufficient to care for the metabolic needs of the tissues. In the patient in shock, the flow of blood was markedly reduced. The circulation decreases as a result of apprehension, embarrassment and fear. The prospect of losing consciousness under anesthesia, anticipation of operation and even the anxiety caused by a casual remark of the operating surgeon cause a reduction of blood flow. Since a diminished blood flow is characteristic of shock and since fear causes a decrease in blood flow, it is possible that the harmful result of fear is due to its effect on the peripheral circulation.

Studies were made on a patient who presented the classical picture of shock but in whom no organic cause for this condition could be found. During the course of these studies, in spite of the fact that no medical treatment was instituted, the patient recovered from her shock-like condition. The blood flow through her hand increased as the observations were being made.

Recognition of fear in the patient is frequently difficult. Physiological expressions such as pallor, thirst, cardiovascular stimulation and gastro-intestinal inhibition may be clues to the real feelings of the individual.

In the treatment of fear, emphasis should be placed on the personal relationship between physician and patient. The advantages to be obtained from religion depend upon the patient's previous conditioning. It is possible that the emotion of fear may be displaced by other thought processes, although it is difficult to make the patient forget his fear. The use of sedatives in mild forms of fear is desirable but may be useless in extremely agitated patients. The intravenous use of alcohol for such individuals is suggested.

These observations on the effect of emotional states on the peripheral circulation suggests a possible mechanism for the clinical impression that fear has a deleterious influence on the general condition of the patient. Every patient, whether he admits it or "bluffs it out," is in a state of fear. Attempts should be made to recognize the presence of fear and to mitigate its harmful effects.

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* Presented at the joint meeting of the Section on Neurology and Psychiatry and the Society, March 24, 1937.

Normal Pregnancies and Deliveries in Bicornate Uteri.—Although bicornate uteri have been known to exist for several centuries, it was not until a few decades ago that interest was aroused in the occurrence of pregnancy in these malformed uteri. It was Mauriceau and Vassal who, in 1669, recorded the first case of pregnancy in a rudimentary horn of a bicornate uterus. It was not until the beginning of the twentieth century, however, that interest in this condition again came to light, although occasional cases were reported before this. An excellent review of the subject was made by Van der Velde in 1915, and in 1922 Miller collected 54 cases of uterus didelphys. In this series there were 67 pregnancies, of which 61 per cent went to term. His studies included only those cases of separate uterus and cervix, and not the bicornate types (uterus bicornis, unicollis, septus, etc.). In reviewing the literature from 1922 to the present writing (July, 1936), we have found reports of 246 cases of malformations of the uterus, including double uterus and cervix (uterus didelphys), double fundus and one cervix, and uteri with rudimentary horns. There are, no doubt, others which we have missed. . . .

From the foregoing it is evident that pregnancy in bicornate uteri is not rare; on the contrary, every physician doing a gynecologic and obstetrical practice must keep it in mind in every patient he sees. It is because of this and of our blunders in two such cases that we here present two cases of bicornate uteri. . . .

Comment.—Our first case represents an easy mistake to make. Where there is a suggestive history of gonorrhea followed by menorrhagia, and in a pelvic examination a mass is felt in one adnexal region, one is prone to jump to the easier and more common diagnosis of a tubo-ovarian pathologic condition. However, it is of interest to note that this patient bad had three normal pregnancies with spontaneous deliveries at term. The course of the second case is a fairly common one in such anomalies. Ectopic pregnancy, with subsequent perforation and hemorrhage, has been reported over 40 times in the 246 cases we have reviewed.

Summary.—Two cases of bicornate uteri verified by laparotomy in which pregnancies and spontaneous deliveries have occurred. In the first case a spontaneous abortion had occurred, and in the second an ectopic tubal gestation had ruptured. . . . . .

Abstract of case report by M. G. BEAVER, M.D., Redlands, and K. H. ABBOTT, M.D., Ontario, *California and Western Medicine, July, 1937, p. 41.*

MEDICAL ANNALS

of the

DISTRICT OF COLUMBIA

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TO THE MEMBERS OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA:

I feel deeply the responsibility you have placed upon me by electing me to the highest office in our Society and at the same time appreciate the great honor bestowed upon me—the greatest that can be bestowed upon any member. Mere words cannot express my appreciation and I can only hope that a year hence you may be able to say truthfully that my task was well done.

I promise not a "New Deal" but I do promise to give the best that is in me to the service of the Society and in the interest of keeping the practice of medicine on the high plane that our predecessors have placed it. This promise, however, is futile unless I have the loyal support of the various committees and of each member of the Society.

Constructive criticism and new ideas I hope you will give freely; especially is the attitude toward current medical problems of the younger members sought. The rapid changes and the tendency to socialize the practice of medicine demand deep and careful thought upon the part of each of us but particularly upon the part of the younger members as the brunt of this new burden will be largely upon their shoulders and they will be more affected by the new order than will the members who have been in the practice over a longer period of time. The latter I know will give freely and willingly of their experience and knowledge in helping us over the rough places.

We hear today a great deal about the medical care of the poor. I have been connected with hospitals in some capacity for 38 years and I am sure in all these years I have never heard of any doctor of medicine refusing to give freely of his time and skill to the indigent without thought of remuneration. The community, of course, must provide food, shelter and the work shops for us, but politics must never be brought into the picture in any form that will deny the patient the right to select his own doctor. For should that time arrive then will the practice of medicine begin to take a backward step. This warning has been given by my predecessors and it may be that the component state societies, the Medical Society of the District of Columbia, as well as the parent association, the American Medical Association, have not accepted fully the opportunities present to keep those who are engaged in the practice of medicine free agents and unhampered by politics in any form.

I am still of the opinion that we should fight to the last ditch to uphold the dignity of the profession and the honor of such men as Lister, Pasteur, Hunter, Semmelweis, Reed and all the others who gave their all for suffering humanity.

I beg your support and your constructive criticism and your patience in the coming year. And again let me express my appreciation of the honor of serving you.

THOMAS EDWIN NEILL.

THOMAS EDWIN NEILL, M.D.

Dr. Thomas E. Neill, who becomes the seventy-first President of the Medical Society of the District of Columbia, was born in Virginia, January 22, 1879, the son of Mary A. Francis and Dangerfield Fauntleroy Neill. The latter served in the Sixth Virginia Cavalry during the Civil War. Dr. Neill spent his early days on his parents' farm. He became an employee of the Massachusetts General Hospital, where he had an unusual opportunity to fit himself for the study of medicine. In 1904 he entered the Georgetown University School of Medicine,

THOMAS EDWIN NEILL, M.D.

President, The Medical Society of the District of Columbia, 1937–1938

CAT.

receiving his degree in 1908. He became noted for athletic activities, serving during his freshmen year as guard on the football team and as a member of the crew which met with much success at the Poughkeepsie contests. Dr. Neill served as extern at Garfield Memorial Hospital during his senior year in medical school, for 15 months as intern at Georgetown University Hospital and 13 months at Columbia Hospital. He began the general practice of his profession in Washington in 1910; later in 1913 becoming associated with Dr. James F. Mitchell, at which time his practice became limited to general surgery and the specialties of gynecology and obstetrics.

During the World War he served as Major in the Medical Corps, United States Army. In 1919 he resumed his practice limiting his work to general surgery and gynecology. At present he holds the position of Senior Gynecologist to Garfield Memorial Hospital and Consulting Gynecologist at Emergency Hospital. In the latter hospital he is a member of the Board of Directors. He is a Fellow of the American College of Surgeons and of the American Medical Association.

Dr. Neill married Eleanor Emerson of Washington, D. C., in 1913. They have one daughter, Eleanor Virginia.

His club memberships include Chevy Chase and Metropolitan.

THE SYPHILIS PROBLEM

This issue of the Annals is devoted largely to a consideration of the subject of syphilis. The articles were not especially selected, but their origin is significant in that they come from isolated sources and indicate some of the various agencies working in the same field. One is illustrative of original laboratory studies being pursued in a private institution, another reviews the activities of an outpatient clinic of a community hospital, still another deals with the efforts toward eradication by the local Health Department, and one comes from a federal agency concentrating on the same problem. As regards our local problems perhaps better results could be obtained by better coördination of resources and activities. All of the large community hospitals conduct excellent outpatient clinics for the diagnosis and treatment of syphilis. These hospitals are working as units more or less independent of each other and of the Health Department. This isolation of forces is the greatest weakness of the antisyphilis army. To exert the greatest influence in the war against syphilis will require close coöperation of the community hospitals, the Health Department, the Medical Society of the District of Columbia, the various social agencies concerned, and the individual physician.

There should be some coördinating unit. This logically is the Health Department. Each community hospital should work under the coördinating guidance of the Health Department. On the other hand, the health Department should not attempt to compete with the hospital clinics but to supplement them. In other words, the Health Department should consider each hospital clinic as a part of itself. By so doing it will obtain gratuitously the services of a large number of physicians well qualified for the diagnosis and treatment of syphilis. It is believed that these physicians would welcome a liaison with the Health Department. Toward this end conferences should be inaugurated for the purpose of collecting data of existing conditions, for detecting weaknesses, and for outlining and instituting the course to be pursued.

A few figures will show the great amount of work now being done in some of the hospital clinics in the treatment of syphilis alone. During 1936 there were 318 children with this disease under treatment in the syphilis clinic of Children's Hospital; these children paid 5,692 visits to the clinic during the year. At Georgetown University Hospital 537 patients with syphilis were treated in 1936; these patients appeared at the clinic a total of 5,984 times. At the Gallinger Municipal Hospital 610 patients were under treatment in the syphilis clinic in 1936; they paid 9,559 visits to the clinic. At Garfield Memorial Hospital 132 syphilitic patients were treated during 1936; at Providence Hospital, 206; at George Washington University Hospital, 62; at Emergency Hospital, 146; at Columbia Hospital, 70; and at Freedman's Hospital, 517. One clinic is now considering the advisability of adding a night syphilitic clinic for semi-indigent patients who have to work during the day to earn a meager living and who, therefore, cannot attend the day clinic.

It is believed that the standard of treatment of syphilis in these various clinics is adequate. The main difficulty has been in getting patients to return to the clinics regularly for treatment. This is just where the Health Department could be of great service. If the Health Department would lend a hand in getting delinquent patients to return for treatment by means of social-service follow-up the work done in the clinics would be infinitely more effective. Furthermore, the Health Department would then have records of the greatest possible number of indigent and semi-indigent individuals in the District of Columbia who are known to have or to have had syphilis. Four things could be done by securing the confidence and coöperation of those in charge of these clinics: (1) Standardization of treatment, (2) supplying necessary chemicals for the treatment of indigent patients when and where the supply is inadequate, (3) placing laboratory facilities at the disposal of the clinics when necessary, and (4) most important, providing adequate social-service follow-up. There is no question that the chiefs of these clinics would welcome coöperation and leadership from the Health Department along these lines.

As an obstacle to the promulgation of these proposals it has been stated that it is illegal to use Health Department funds for helping to maintain "private" institutions. This obstacle should be easily overcome, as has been done elsewhere, and certainly a liberal interpretation alone would obviate the difficulty. Any funds so expended would not be used to maintain the community hospitals but merely to make the treatment of indigent patients with venereal disease more effective. Chemicals could be supplied to the hospitals when needed for the treatment of designated patients on the basis that the Health Department were merely requesting the hospitals to treat these patients in the name of the Health Department. So far as social-service work is concerned social workers assigned the task of keeping check on syphilitic patients could merely be assigned to follow patients being treated in one or more of these hospitals. They would continue to work under the direction of the Health Officer, and the Health Department headquarters would be their base of activity.

It is hoped that such coöperative efforts as are here suggested will be inaugurated. For this purpose leadership is required. Perhaps the Health Department will supply this.

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TRANSACTIONS OF THE SOCIETY

Stated Meeting, May 19

(Continued from June issue)

Reports of Committees

Committee on Public Health

SUBCOMMITTEE ON DEAFNESS PREVENTION*

This committee might very properly have busied itself with several aspects of the problem of deafness prevention, but it has seen fit to concentrate its effort upon that one phase which seemed to it most important, most urgent and most promising in results, viz., the education of the hard of hearing children in the public school.

The committee has taken steps to inform itself of the prevailing practices in other parts of the country and of their successes and failures, and through its chairman has held conference with persons having a special knowledge of conditions especially in this city, viz., Dr. J. A. Murphy, Chief Medical Inspector of Public Schools; Mrs. Grace W. Atherton, in charge of the Department of Speech Defects and Lip Reading, Public Schools; Miss

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* Presented, May 19, 1937. Recommendations contained therein now under consideration by the Executive Committee.

Betty C. Wright, Executive Secretary of the American Society for the Hard of Hearing; and Dr. Carroll E. Palmer, Physician-in-charge of Child Hygiene, United States Public Health Service.

Washington is far behind other cities of the country in this phase of social work. It is doubtful if there is another city in the whole country which is doing so little for hard of hearing children in the public school. Most cities of comparable size have complete programs; and even small communities partial programs. In several states provision is made for routine audiometric examination of all school children. In some states such an examination is compulsory by law. In more than half the cities lip reading teachers are available. Washington has no program.

It is, of course, absurd to say, as some have done, that conditions are exceptional here, and that Washington has not a large contingent of hard of hearing children in the public school in need of special care. Averages in such matters have been found to prevail much the same in different surveys made in all sections of the country.

Authorities differ as to the percentage that has defective hearing, and as to the exact proportion that need special instruction, because of different criteria adopted by different examiners.

School surveys in various parts of the country made by the use of 4 A Audiometers have generally resulted in an average of about 5 per cent of children showing some defect in one or both ears. But this is too high an estimate to represent true conditions. Many cases are put down as defects due to a poor technic, and unskillful examination. Many of the cases are temporary, and subsequently clear up.

Suppose we adopt a definite and more stringent criterion and set aside as having a notable loss of hearing only those cases which show a defect amounting to 10 decibels in both ears, or in the better of both affected ears. This condition will catch at least 1 per cent of all school children examined. Now it is certainly fair to claim that in half of these cases, i.e., in 1 out of every 200, the defect is of such degree that lip reading instruction is indicated. In the city of Washington there are in the neighborhood of 90,000 pupils. That would make about 450 which need lip reading instruction.

On inquiry I learned that in the past year, there were only 2 lip reading teachers available in the public schools of Washington and only 15 pupils received lip reading instruction.

Is a special educational program for the hard of hearing child beneficial? Does it actually bring results? If education in general is desirable, then education of the hard of hearing child is doubly desirable; because such children not properly instructed become a burden and extra expense to the state.

"The happiness and stability of the nation," said Senator Pepper of Florida, in a recent radio address, "depends upon the proper education of children. We cannot afford the expense to society of not educating children that are handicapped in limb, eye or ear."

This is particularly true of the hard of hearing and the deaf. This class of defectives are, of course, not mentally defective as was formerly believed, but are exceptionally alert, ambitious and responsive to educational efforts. The deaf and hard of hearing, are in fact the only class of defectives which have taken their problems in their own hands and attempting themselves to solve them. In this country they are organized as the American Society for the Hard of Hearing. Physicians, especially otologists, have nothing but praise for the benefit accomplished by this great organization. Through its constituent local league it has expressed itself as strongly in favor of a program for the education of the hard of hearing of this city, and has earnestly besought our Society for coöperation toward this end.

There is every reason to believe that an educational program will bear fruit. Great advance has been made in recent times in two directions; that make this more than ever possible. I refer to the introduction of the electric audiometer by which means hearing defects are accurately measured, and the electric hearing aids, by air and bone conduction by means of which remnant hearing can be successfully utilized.

Admitting the need, there is always the serious question of cost, and the difficulty of securing the financial appropriation for the execution of a program. Here let me repeat what has already been said, namely, that no community can afford not to provide this kind of care, and that is true from a strictly financial as well as a moral standpoint.

Estimates show that the cost of educating children with defective hearing is, on account of retardation in class and repetition of grades, actually greater than it is when provision is made for the special education to keep them abreast with good hearing pupils.

Besides, hard of hearing children that fall behind their classes and are segregated from their fellow pupils are apt to become morose, suspicious and develop other personality obliquities, affecting their character as citizens, the costs of which to the state are not definitely measurable.

Your committee does not expect and would not demand off-hand a large appropriation, such as that desired by the enthusiasts for a better education of the hearing defectives. But it would like to see a beginning, and it hopes that this Society will stand behind a modest and reasonable recommendation.

The greatest need at present is not for the slightly hard of hearing, nor for the completely deaf (the latter requiring special schools), but that considerable contingent of severely hard of hearing children who, unless receiving special instruction, would get no instruction and have to be segregated in special schools with completely deaf children, which would be very bad for them.

For the severely hard of hearing it is necessary that they be taken care of by the organization of special conservation of hearing classes; taught in rooms, specially equipped with group hearing, and under the care of special broadly educated lip reading teachers.

Conservation of sight classes are now in operation in this city for children with poor vision; and special clinics are provided for children having dental defects. Are not children with bad ears as worthy and deserving of special care as children with bad eyes and bad teeth?

The committee, therefore, recommends that the Medical Society of the District of Columbia endorse the organization of a special conservation class for the severely hard of hearing of the public schools of Washington, and that it pass resolutions setting forth that:

Whereas, Washington is far behind most cities in the special instruction of the hard of hearing in the public schools; and

Whereas, Because of recent advances in methods of measuring hearing and of aiding hearing, such teaching is productive of much good; and

Whereas, It is actually more economical in dollars and cents to give proper instruction to the hard of hearing, than to neglect it; and

Whereas, Analogous provision has already been made for children with defective vision and with defective teeth; therefore, be it

Resolved, That the Board of Education be requested to set aside rooms appropriate for the use of a Conservation of Hearing Class for the severely hard of hearing, and that a sum be allotted sufficient to pay for the services of 1 physician in charge of the department, 3 competent broadly educated lip reading teachers, and 1 technician capable of making audiometric examinations, and for the purchase of equipment consisting of electrical group hearing aids, and simple instruments for the examination of the ears.

Walter A. Wells, *Chairman*
Jeter C. Bradley
Harry F. Davies
William C. Meloy
Subcommittee on Deafness Prevention

SUBCOMMITTEE ON CONSERVATION OF VISION*

1. According to the suggestions at the meeting of the Committee on Public Health on July 15, 1936, the committee elected Dr. William Thornwall Davis to act as Chairman of the Subcommittee on Conservation of Vision and to act as liaison officer between the Washington Chapter of the National Society for Prevention of Blindness and the National Library for the Blind. This has been carried out in many cases with advantage to the Medical Society of the District of Columbia and the two mentioned organizations. This is of considerable value and it would be well if it could be continued.

2. There have been no reports by the members of the committee of the use of drugs or medicines in treating eye diseases by those other than ophthalmologists. Therefore, no cases have arisen requiring action.

3. It may be noted that the law for prevention of gonorrheal ophthalmia has been passed by Congress in April, 1937. Undoubtedly the activity of the Committee on Legislation assisted in passing this important law.

4. Effort has been made and should be continued through the coming year to obtain statistics in the public schools on the incidence of myopia. Unquestionably important data could be secured of value in determining the etiology of this condition. It is urged and recommended that this study be continued as it would be necessary to continue it over a period of years to be of value.

5. Nothing has been accomplished so far in obtaining a law preventing the use of air rifles in the District of Columbia. More important legislation was taken up by Congress.

6. Some effort has been made to emphasize before the Society as a whole the necessity of immediate treatment of children with squint to prevent deterioration of vision in the squinting eye.

7. Effort has been made to encourage the Health Department to secure the visual acuity of children immediately upon entering school.

8. Dr. J. Beaty Griffith wrote a letter to the Chairman of this Subcommittee, saying that the Washington Council of Social Agencies is interested in studying the needs of the blind, such as manual training for the blind, provision of transportation for the blind to attend clinics when necessary, etc. Coördination between these two agencies is of undoubted value.

William Thornwall Davis, *Chairman*
Carl Henning
J. Beaty Griffith
LeRoy W. Hyde
Subcommittee on Conservation of Vision

SUBCOMMITTEE ON VENEREAL DISEASES*

The Subcommittee on Venereal Diseases, after a careful study of the venereal disease problem, as it is presented to the private physician, the hospital clinics and the public health clinics of Washington, has decided upon some definite recommendations which we believe will make a definite start toward alleviating the venereal disease situation in the District of Columbia.

To those interested in the subject we most heartily commend the report made by your committee last year, and presented to the Society on May 20, 1936, by Dr. Russell J. Fields. This is a very comprehensive report, and we are thoroughly in accord with it. In this report we shall deal more with the practical application of the remedy to the matter in hand.

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* Report accepted by the Society, May 19, 1937.

* Adopted by the Society, May 19, 1937.

In the first place, it must be understood that no campaign can be successfully carried on against these evils without funds. We understand that funds can be allocated to the prevention and treatment of venereal diseases in the District of Columbia. Working on this assumption, we wish to make some recommendations which can be carried out at a minimum cost. By making a few alterations in our present setup, this plan can be put into effect without the added expense of more buildings and equipment.

This problem is essentially a public health problem, and must be so considered. There are certain phases of the problem which can be handled only by the United States Public Health Service. There are other phases, such as the greater part of the treatment, which must be carried out by local doctors. We are convinced that a very close and amiable relationship must exist between the members of this Society and the public health office in order that the best results may be obtained in carrying out this campaign. Your committee has met and discussed this entire problem with Dr. George C. Ruhland, and we are convinced that the Health Department can be depended upon to do its part at all times.

We now come to the fundamental part of the problem, viz., the diagnosis and treatment of venereal diseases. Based on the economic status of the patient seeking treatment, this problem may be considered under 3 main groups, viz., those cases going to (1) private physicians, (2) established Public Health Clinics, and (3) established hospital clinics.

1. *Those cases going to private physicians.* Obviously all private cases must be diagnosed and treated by such methods as are best suited to the individual physician. Each physician should and will treat his cases as he sees fit. Laboratory work to be done by the private doctor or his pathologist and paid for by the patient. There will be certain cases requiring long drawn-out treatment, particularly luetic cases where repeated tests will be advisable, the cost of which may be beyond the means of the patient to pay. The Public Health Department should stand ready to make any and all such tests on the request of the physician. We are not in favor of free drugs and arsenicals to private physicians to administer to private cases. All private cases should be reported to the Health Department by number, the name and address to be supplied only in cases where treatment is suspended before the infectious stage of the disease has passed. The Health Department should supply each physician with necessary blanks and franked envelopes for these reports. Also, a small fee for making such reports is desirable. The Health Officer is in accord with these recommendations.

2. *Those cases going to established Public Health Clinics.* These clinics are being conducted by the members of our Society under the direction of the Health Department for the care of the indigent. This group is well cared for and no recommendation by this committee is necessary.

3. *Those cases going to established Hospital Clinics.* Here lies our real problem, and the one that needs to be solved, and solved at once. We are all more or less familiar with the so-called G.-U. Clinics as they have existed in our local hospitals for years. The conditions under which these clinics have operated in the past and operate now are unsatisfactory to the hospital, to the doctors working in them and to the patients attending them. Your committee has met with representatives from all these clinics, and has been impressed by an enumeration of the needs of these clinics. May I cite some of them?

1. More doctors needed in every clinic.
2. More Social Workers needed.
3. Some means of forcing patients to continue treatment.
4. Standardization of treatment.
5. Unlimited free and accessible laboratory service.
6. Standardization of tests (G. C. and syphilis).
7. Better system of records.
8. Free drugs, including arsenicals and heavy metals.

As we see the situation at present, two facts stand out: (1) The hospitals are furnishing workable quarters for clinics; (2) the public is furnishing patients to be examined and treated.

Further than this little can be said by way of commendation in the manner of caring for acute cases of gonorrhea and syphilis in our indigent cases who seek relief in our hospital clinics at the present time.

Your committee recommends:

1. That a subsidy be granted to the hospitals from Public Health funds to carry on this purely public health measure.
2. That the hospitals continue to house venereal disease clinics as in the past.

Such an arrangement could be carried on at a very low cost; and with the united efforts of the Public Health Department working with a committee from the hospitals, the following recommendations could be carried out to the mutual satisfaction and best interests of patients, doctors and hospitals:

1. A satisfactory personnel, including doctors, nurses and social workers, could be obtained and depended upon to carry on the work by paying the proper salary in each case.
2. All laboratory work should be done by the Public Health Laboratory, specimens to be collected each day and reported the following day. This would relieve the hospitals of this burden, and insure a uniform standardization for all examinations.
3. A uniform standard form of treatment could be decided upon and carried out in each clinic.
4. All drugs to be furnished free to each clinic by the Health Department.
5. A uniform system of records could be worked out and checked daily to insure continued treatment, and prevent patients from shopping around from one clinic

to another. Such a system is being worked out now in the Central Admitting Bureau for Hospitals.

6. The exercise of police power on the part of the Health Department to require infectious cases to come for treatment.

H. N. Dorman, *Chairman*
Norvell Belt
James M. Fadeley
F. A. Reuter
Subcommittee on Venereal Diseases

SUBCOMMITTEE ON SANITATION*

The Subcommittee on Sanitation has met with representatives of the Health Department, and has discussed the problems of sanitation in the District of Columbia with them. This report is based on that discussion.

1. The food, milk, water and ice supply is satisfactory, and no problems exist there. All ice used in the District of Columbia is artificial, and is entirely satisfactory. Wells are not a problem in the District of Columbia, as most of the dwellings are using the District water supply.

2. Prevention of the distribution of the saliva-borne diseases, in public eating houses, has been studied extensively, and certain regulations have been adopted. (Copy appended.) Where previously the dishes in public eating houses showed 150,000 bacteria per utensil surface (about 4 square inches) before washing, and 50,000 bacteria per utensil surface after washing; with the present method of washing the dishes with hot water, or by the use of chlorine solution, not more than 500 bacteria per utensil is allowed.

3. Fly breeding continues to be somewhat of a problem; the flies breed especially in and around open garbage cans. Regulations require that the cans be kept covered, but this is frequently ignored.

4. Sewage disposal. There has been consideration of activated sludge treatment, and chemical treatment, of the sewage. It was decided to treat the sewage by sedimentation, which reduces the oxygen consumption by about one half; and a sedimentation plant has been built at Blue Plains, Md. The sludge from this plant is to be digested and shipped to Lorton, for filling. This plant will be in operation in a few weeks to a few months.

Privies are not a problem in the District of Columbia, as most of the dwellings are connected with the sewer system. There are not over 1,500 privies in the District of Columbia.

Public Comfort Stations have received consideration; and the District of Columbia seems to be behind other cities on this problem, as there are only two of these stations in the District. There is rather urgent request for 6 additional stations; but there is no money for putting in such stations, and the need does not seem to be urgent.

5. Waste disposal. Deficiency of funds is an important item here.

Combustible trash is burned in 2 high-temperature incinerators: 1 in Georgetown and 1 in southeast Washington. Tin cans go in with this trash, and after being burned out, are thrown out on the dump, and are rolled flat with a roller. These 2 incinerators have about reached the limit of their capacity now.

Ashes are used for filling; and there is no difficulty in disposing of them for that purpose.

Garbage. That from hotels and other large eating places is hauled away by the farmers, using water tight wagons, and used for feeding to hogs. The rest of the city garbage is collected by the District wagons, and hauled to the collecting station on New Jersey Avenue, southeast, From here, a large part of the garbage is taken by the farmers, and used for feeding to hogs. What is left is shipped down to the garbage reduction plant at Cherry Hill, Va. This plant has been rehabilitated, and is kept in operation, so it may at any time take care of the entire amount of garbage, in case of breakdown in the plan of having the farmers haul it away. The present satisfactory price of garbage grease makes it rather worth while to operate the reduction plant. There is some complaint of the odor in the neighborhood of the collection station, in the southeast section of the city; and some of the citizens have urged that the station be taken away from there—and put on Connecticut Avenue!

A high temperature garbage incinerator is considered the last word but the cost is prohibitive.

Some of the apartment houses are putting in incinerators, to burn their combustible waste and garbage; these incinerators are satisfactory.

6. Mosquito breeding is somewhat of a problem during the summer months; the sewer catch basins (13,000 in the District of Columbia) are the most important breeding places for mosquitoes, and are oiled once a week during the summer.

7. Abattoir. The problem of a public slaughter house within the District of Columbia is acute at this time. It is being studied, and will be solved satisfactorily.

8. Flood control is a great problem, and is being studied widely and intensively. Floods will flood the sewers in the District, and may put the sewage pumping stations out of operation.

The Subcommittee commends the Health Department of the District of Columbia on the efficient manner in which the sanitary problems are being handled.

Eugene R. Whitmore, *Chairman*
William J. Mallory
John Bayne Marbury
Subcommittee on Sanitation

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* Report accepted by the Society, May 19, 1937, and resolution contained therein adopted.

COMMISSIONERS
of the District of Columbia
Executive Department
Washington, D. C., April 26, 1937.

ORDERED:

That the following regulations are hereby adopted:

Regulations to Prevent, by the Disinfection of Eating and Drinking Utensils, the Distribution of the Saliva-borne Diseases, in Public Eating and Drinking Places.

Sec. 1. Eating and drinking utensils, including silverware used for service in eating and drinking places or any other place where food or drink is served, shall be thoroughly cleaned and disinfected between each service or use.

Sec. 2. The utensils shall be thoroughly washed in the compartment containing the soapy wash water, which shall be changed at sufficiently frequent intervals as to keep it reasonably clean and to maintain an adequate detergent content at all times.

Sec. 3. The standard bacteriological requirements for washed and disinfected eating utensils used to serve the public shall be not more than 500 organisms per 4 square inches of any utensil surface area, or 500 organisms on the inside and outside ½ inch rim surfaces of cups or glasses, or 500 organisms per spoon, each by the multiple test procedure.

Sec. 4. Disinfectant or germicidal solutions of chlorine as well as other germicidal compounds may be used if approved by the Health Department.

Sec. 5. Any person who violates any of the provisions of these regulations shall be punished, upon conviction thereof, by a fine not exceeding $50.00 for the first offense, and for each subsequent offense by a fine not exceeding $100.00 or by revocation of license through the License Revocation Board.

Sec. 6. Regulations to govern the common use of drinking cups in the District of Columbia as of December 3, 1915, is hereby revoked.

Sec. 7. These regulations shall become effective June 1, 1937.

Approved Methods of Operation

1. The Health Department approves the following technical methods of operation:

2. The person or persons responsible for the operation of eating or drinking places shall have the option of resorting to the adoption of any one of the several following methods for the cleansing and disinfection of utensils.

Mechanical or Machine Washing

3. All mechanical washers while in operation should have a mechanically regulated continuous and adequate supply of detergent so that the concentration of the detergent shall be sufficient for a thorough cleansing process. This thorough cleansing, consisting of the removal of fats, grease, and other débris, is a prerequisite for a low bacterial count essential to the protection of public health.

4. When the machine is of but 1 compartment the washing water shall be maintained at or about 170°F. for disinfecting purposes and contain sufficient soap or inorganic detergent to thoroughly cleanse the utensils. The dishes shall be exposed to the cleansing and disinfecting wash and the final rinse for at least 3 minutes and air dried.

5. When the machine is of 2 or more compartments, the water in the first compartment shall contain adequate soap or inorganic detergent and shall be changed at such frequent intervals as to keep it free from visible dirt, and the water in both the first and second compartments shall be maintained at a temperature of not less than 170°F., or the washing water in the first compartment shall be hot water—120°F.—contain an inorganic detergent and shall be changed at such frequent intervals as to keep it free from visible dirt, and the second compartment shall contain a clean solution of a chlorine disinfectant in the proportion of 200 p.p.m. and at no time less than 50 p.p.m. of available chlorine, and by either of these methods the utensils shall be exposed for at least 3 minutes.

Hand Washing

6. Eating utensils may be washed in hot water containing soap or an inorganic detergent of such concentration as to thoroughly cleanse the utensils, and the washing water shall be changed at sufficiently frequent intervals as to keep it free from visible dirt, and subsequent to the washing and cleansing process the utensils in a rack shall be either immersed in water of a temperature not less than 170°F. or in a chlorine disinfectant solution in the proportion of 200 p.p.m. and at no time less than 50 p.p.m. of available chlorine, for at least 3 minutes.

7. Beverage glasses may be cleansed and disinfected by the 3-compartment method. The used glasses are first drained of their beverage content, next washed preferably by the brush method in the first compartment containing inorganic detergent and hypochlorite, then placed in a rack and immersed for 3 minutes in the second compartment containing hypochlorite, and finally rinsed in the third containing running water. The chlorine disinfectant in compartments 1 and 2 shall be in the proportion of 200 p.p.m. and at no time less than 50 p.p.m.

8. The soapy wash water shall be changed at frequent intervals, visibly clean at all times, and at no time contain more than 36,000 bacteria per cc.

9. After the utensils have been cleansed and disinfected they should be handled and cared for in a sanitary manner so as to avoid their re-contamination.

EXCERPTS, HEALTH DEPARTMENT NEWS LETTER ON CURRENT ACTIVITIES*

June 26, 1937

C. F. Browning, *Public Health Engineer*

Air Pollution is becoming a problem in Washington. Recently a number of complaints have been received concerning carbon monoxide and fumes from busses. These are mostly from the areas where street car service was discontinued and replaced by bus service, but complaints also have been received from the areas which have bad bus service for a long time. Undoubtedly, there is cause for the complaints. Investigations have shown that carbon monoxide in amounts which are near to the known toxic limits are present in some sections during rush traffic. Tests made while following busses show toxic amounts present in the auto following the busses. The fumes are unquestionably present in annoying and perhaps harmful concentration. Very little is definitely known about their harmfulness. We know they are offensive and as such constitute a nuisance. Electric busses have proved satisfactory in some other cities. The cleanliness and comfort afforded by this type of conveyance should weigh considerably in their favor.

Air Conditions in places of public assembly are now being inspected by the Bureau of Sanitation, and tests are being made for both the physical and chemical properties of the air. Any unsatisfactory conditions that are found are reported and steps are taken to correct them. The most difficult problem at this time is the cooling of air-conditioned buildings. A number of buildings are being cooled more than is necessary. There should never be more than 15 degrees difference between the temperatures of the air outside and the air inside of the building. A 10-degree difference is recommended during hot weather.

The Mosquito Control Project is again at work after a delayed start. Some difficulty was encountered in obtaining approval of the WPA project, but it was finally received and work is now under way. The project is being supervised by the United States Public Health Service and the field control work is being performed by the various government agencies on their own reservations, and the District of Columbia Sewer Division on public property. Any complaints regarding mosquitoes should be referred to National 5710, Branch 426.

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* Newer problems awaiting solution. Ed.

THE MEDICAL SOCIETY ACQUIRES PROPERTY

On June 28, 1937, completion of purchase was made of premises, 1710 M Street, N.W., which immediately adjoins the Society's property to the east. This adds 3,746.61 square feet to our possessions, making a total of 10,529.61 square feet, inclusive with the present Medical Society structure. The total frontage on M Street is 79.17 feet. The advantages of making this purchase at this time should be immediately apparent. The favorable price obtained for property makes the appreciation in value quite sure with coming years. The building is now subdivided into 5 apartments, all of which are rented. The income is sufficient amply to take care of all carrying charges. Our present building with its auditorium of 500 capacity and other facilities barely meets our present needs. Certainly within the next 20 years it would seem there will be need for expansion. This may be done by extending our present floors through to the next building. The possibility of a new enlarged structure on the two lots at a future date, with an enlarged auditorium and other accommodations for the growing demands of our scientific meetings, is entirely within reason and will afford opportunity of rendering greater service to the community. Those who had the foresight in advocating the gaining of this land with greater facilities at this opportune time and pushed the plan through to a successful issue deserve the commendation of all who have the best interests of the local profession at heart.

Recent Addition to Medical Society's Property

THE DOCTORS' HOSPITAL, INC.

Plans have advanced sufficiently to announce the proposed erection of an institution of 250 beds with ample facilities for expansion on property extending between the Washington Medical Building on the east and the Columbia Medical Building on the west, on Eye Street between Eighteenth and Nineteenth Streets. The part of the project that should appeal to all members of the profession is that in essence it will be a hospital "by Doctors and for Doctors." The stock is available according to prospectus, "to members of the medical, dental, and allied professions." No lay board of management will be involved.

In the offering of the stock there has been a provision for a wide distribution among the profession, no one person being given opportunity to have a large controlling share:

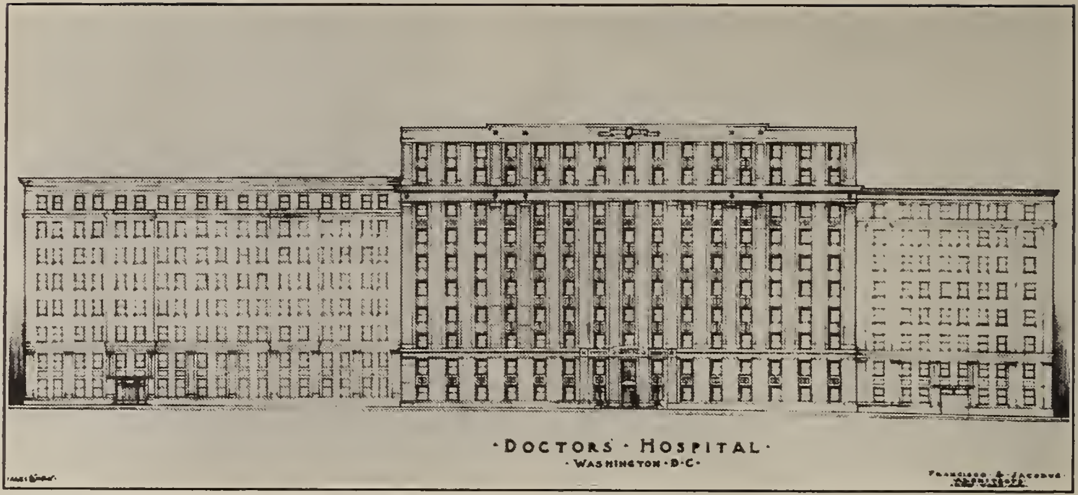
> "This stock is offered by the Company, and may be subscribed for only through its offices, 1835 Eye Street, N. W., Washington, D. C. The offering is strictly limited to members of the medical, dental and allied professions. Individual subscriptions limited to maximum of 100 shares; minimum subscription 5 shares."

Quoting further, showing safeguards placed for the highest type of medical and surgical practice we note the following:

> "The facilities of The Doctors' Hospital, Incorporated, will be restricted to physicians and dentists in good standing in their local medical and dental societies, who have been approved by the Board of Directors of The Doctors' Hospital, Incorporated. Each practitioner will be issued a courtesy card for the period of 1 year, which will be automatically renewed unless otherwise decreed by the Board of Directors of the institution. Physicians and dentists from outside of the District of Columbia will be allowed to practice in the hospital, provided they measure up to the same requirements as those for the members of the Medical Society of the District of Columbia and have been approved by the Board of Directors."

There are to be no promotion charges. The citizenry will profit; note the following excerpt:

> "It will offer to the public and to the medical and allied professions in the District of Columbia hospital facilities of a wide and adequate scope which will rank with the best in the United States. These facilities at a moderate price will be in the greatest demand in the District of Columbia in the near future."



Washington Medical Building (Right); Columbia Medical Building (Left); Architect's Conception of The Doctor's Hospital to be erected—Height 10 Stories—Joining the Present Structures

The officers of the corporation: Drs. Charles S. White, *President and Director*; Edward L. Morrison, *Vice President and Director*; Charles W. Hyde, *Treasurer and Director*; Oscar B. Hunter, *Secretary and Director*; Alan J. Chenery, *Director*. The aforementioned are the founders, or those who applied for the charter.

NEWS AND PERSONALS

American Therapeutic Society, Atlantic City, June 4–5: Members of the Medical Society of the District of Columbia who participated:

Dr. Thomas S. Lee read a paper, entitled, "The Value of the Chest Leads in the Electrocardiogram," in a symposium on cardiovascular disease.

Dr. William J. Mallory read a tribute to the memory of the late Dr. Frank Smithies.

Dr. James Alexander Lyon presided at the scientific session held on the afternoon of the fourth.

The present officers include: Drs. Chevalier Jackson of Philadelphia, *President;* James Alexander Lyon of Washington, *Vice President;* Oscar B. Hunter of Washington, is the present *Secretary;* Lewis H. Taylor of Washington, *Chairman of Council*

At the annual banquet held in Hotel Traymore, **Dr. R. Lyman Sexton** exhibited motion-pictures in color taken in Mexico.

Dr. Thomas Madden Foley read a paper, "Fractures of the Tuberosities of the Humerus," before the Tri-State Medical Association of the Carolinas and Virginia. In the July issue of Southern Medicine and Surgery the paper appears in full with discussion by Dr. Alonzo Myers of Charlotte, N. C.

Frank Lee Biscoe, M.D.

(1876–1937)

Dr. Frank Lee Biscoe, an Active Member of the Medical Society of the District of Columbia since April 15, 1903, and a graduate of Georgetown University School of Medicine in the class of 1901, died July 18, 1937, at the Veterans' Hospital, Wadsworth, Kansas, where he was stationed under the Veterans' Administration. Dr. Biscoe practiced his profession in Washington until his entry into the Medical Corps of the United States Army. Following the War he held several responsible positions in various Veterans' Institutions, including Albuquerque, and Fort Bayard, New Mexico, Hines Hospital, Hines, Illinois, serving variously as Commanding Officer, Chief of Medical Service. Dr. Biscoe had many friends in the Washington profession. He never failed to attend the Society's Annual Scientific Assemblies. From time to time he read scientific treatises before the Society; his last appearance was on November 14, 1934, when the title of his paper was "Gastric Syphilis."

Dr. Biscoe is survived by a sister, Miss Annie L. Biscoe of Washington, and a brother, Colonel Earl Biscoe of Honolulu. Funeral services were held in the Western Presbyterian Church with burial in Rock Creek Cemetery, Washington, D. C.

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STUDIES ON OXYURIASIS. III. THE INCIDENCE OF PINWORM INFESTATION IN A GROUP OF 230 BOYS IN WASHINGTON, D. C.

JOHN BOZICEVICH

Division of Zoology, National Institute of Health, United States Public Health Service

Incidence figures for pinworm infestation have been reported for various groups in different parts of the world, but very little work of the sort has been done in the United States. Of the published reports of incidence, many are based on the examination of feces and are merely incidental to special surveys for incidence of hookworm or general surveys for incidence of helminths or intestinal parasites of all sorts. It is well known to those familiar with the diagnosis of pinworm infestation that fecal examinations throw very little light on the incidence of oxyuriasis, since the female pinworm has the habit of crawling out of the anus and depositing its eggs in the perianal region instead of depositing them in the intestinal lumen where they would be sure to pass out in the feces. As it is, pinworm eggs are found in feces rather rarely, and the failure to find them there is a negative finding which is not indicative of absence of pinworms in the sense that negative findings for hookworm or ascarid eggs would be indicative of the absence of hookworms or ascarids. In a comparative study of diagnostic procedures for pinworm infection, Headlee found no eggs by direct smear examination, 3.37 per cent of his cases positive by the Willis flotation technic, and 21.99 per cent positive by anal scrapings. There were, then, between 6 and 7 times as many pinworm cases as were indicated by fecal examinations by a technic suitable for other worm parasites. In the present state of our knowledge the examination of anal scrapings or swabs gives the most dependable information in regard to the presence of pinworm infestation.

I have not yet had time to examine the literature sufficiently to fix the earliest use of swabs and scrapers in the diagnosis of oxyuriasis, but 25 years ago Ruotsalainen used a curette for making anal scrapings, and over 20 years ago Brüning used some sort of a device for examinations of the perianal region for pinworm eggs. There are certain features which limit the value of the scrapers and swabs which have been used in the past, and the N. I. H. swab, developed in the Division of Zoology and described by Hall recently, has proved, in thousands of tests, to be a definite improvement over previous devices. This swab is essentially a cellulose film (cellophane) which is applied by means of a glass rod, and then removed from the rod and examined directly on a slide under the microscope.

In the present study, 230 boys, members of the Metropolitan Police Boys' Clubs of Washington, D. C., were examined by the use of the N. I. H. swab during the period of 3 weeks when the boys were in camp at Camp Brown at Scotland, Maryland. The boys came to the camp in 3 successive groups, each group remaining 1 week. Each group arrived on Sunday afternoon, and the boys were allowed to swim before dinner. It was suggested to them that, just before retiring for the night, each boy should take a shower, and most of them, but not all, did this. The following morning, before the boys were allowed to use the toilets or wash basins, swabs were made, and these swabs were examined during the week that each group was at camp. Only 1 swab examination was made for each boy, since time and the available personnel did not permit of making repeated examinations. Had they been made, they would undoubtedly have increased the number and percentage of positives, as Skrjabin, et al., and Serbinov and Schulmann have established by repeated examinations on different days.

The data for our examinations are presented below by weeks, and cover the number of boys examined, the number positive for pinworms, and the percentage of positives.

	First Week
Number of boys examined	89
Number positive	31
Per cent positive	34.8

	Second Week
Number of boys examined	76
Number positive	16
Per cent positive	21.0

	Third Week
Number of boys examined	65
Number positive	25
Per cent positive	38.5

	Totals
Total number of boys examined	230
Total number positive	72
Per cent positive	31.3

As noted above, the percentage of positives is undoubtedly too low. Repeated examinations regularly increase the percentage of positive findings in any series of this size. This result follows, in part, from an increased likelihood of securing any eggs present by increasing the number of attempts to secure them, and, in part, from the fact that there is a periodicity in the appearance of pinworms on the perineum, a phenomenon conditioned by the successive maturing and migration of females present as these reach the stage of gravid maturity. Another factor limiting our positive findings was the taking of a shower the night before our examination, as this probably resulted in washing off some or all of the pinworm eggs present in the perianal region of some of the infested boys, thereby diminishing our chances of finding eggs in such cases. Data from some of our other work show that strict personal cleanliness results in incidence figures from swab examinations which are definitely lower than the incidence obtained from additions to the same groups when the additional persons are examined on arrival and before being subjected to the same sanitary régime.

The boys at the camp were from 6 to 18 years old, and came from all the principal sectors of Washington, and from groups of both high and low economic-social status. However, the great majority came from the more or less underprivileged groups for which the boys' clubs were instituted. Boys from the same social groups had been examined for intestinal parasites 2 years previously by Dr. J. E. Alicata, and on fecal examinations, in which pinworm eggs would be detected only as they were accidentally present in rare instances, Alicata reported the presence of pinworms in 1.3 per cent of 150 boys from 12 to 16 years old. The indication here, to the effect that the actual incidence might be approximately 24 times as high as the incidence ascertained by fecal examination, is more or less in line with the findings of other workers.

It is evidently a matter of considerable interest, from the standpoint of public health, that over a large section of Washington there is an indicated incidence of pinworm infestation in boys, quite generally unsuspected by most physicians, of over 30 per cent, with evidence indicating that this figure is definitely too low. Findings which will be published in later studies are in agreement with much of the world's literature in showing that clinical symptoms of some importance will be present in a fairly large proportion of infested persons. Our investigations of these boys' club boys are being continued in coöperation with Dr. Leon S. Gordon, Medical Director of the Metropolitan Police Boys' Clubs, and with the other officers of the clubs, in a consideration of incidence, treatment and prophylaxis. The very helpful coöperation of Mr. Jacob Shaffer, President of the Southwest Citizens' Association, has been a great factor in facilitating our work with these boys.

SUMMARY

An examination of 230 boys belonging to the Metropolitan Police Boys' Clubs of Washington, D. C., by the use of the N. I. H. swab for the diagnosis of pinworm infestation, shows that 72, or 31.3 per cent, of these boys were infested with pinworms. The high incidence in this group points to a generally unrecognized public health problem in the form of pinworm infestation, which these findings indicate to be more prevalent in the population of Washington than is generally believed to be the case.

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INTUSSUSCEPTION

SUGGESTIONS FOR OPERATIVE PROCEDURES*

Crenshaw D. Briggs, M.D.

Clinical Instructor in Surgery, George Washington University School of Medicine

In recent years the treatment of intussusception has received a great deal of attention from surgeons and pediatricians alike, and except by a very small minority operative procedure is considered the method of choice in the management of such conditions. Favorable reports have been published from some clinics advocating the use of barium enema. Given under the fluoroscope the enema may be seen in early cases to force back the invaginated portion of bowel. The theoretical advantages of such a method are outweighed by the practical advantages of surgery when one considers that, in the very sick cases, valuable time is often lost in unsuccessful attempts to reduce the intussusception by the use of a rectal injection. One only has to experience at operation the great difficulty frequently encountered in attempting to manually reduce the intussusception in order to realize how futile would be the employment of a barium enema in the hope of avoiding surgical exploration.

That excellent results may be uniformly expected from operation when the condition is recognized promptly is graphically illustrated by Ladd and Gross in review of a series of 372 cases. As other writers before him have done, he stresses the importance of early diagnosis in order to reduce the mortality rate.

The purpose of this paper is to suggest an operative procedure for those neglected cases of intussusception in which segments of the bowel appear to be irreparably damaged.

First, however, it might not be altogether out of place to quickly review the symptoms of this condition, to point out one or two of the possible pitfalls in diagnosis and to emphasize the importance of pre- and postoperative treatment which demand the close coöperation of both surgeon and pediatrician. In Boston and Australia where early diagnosis has been repeatedly stressed, the mortality rate is lower than in any comparable district. These results are in large measure attributable to the fact that the physicians in general practice have been kept intussusception-conscious; the cases have been operated upon early in their course and simple reduction is all that is required of the surgeon.

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* Read before the Society, March 31, 1937.

Statistics show that the most common period for intussusception to occur is between the ages of 6 months and 2 years. The clinical picture produced is a striking one. The patient, who may or may not have had a preceding attack of diarrhea, suddenly develops evidence of severe pain and vomiting. If observed carefully the pain seems to occur in paroxysms. There may be one or two loose stools and these are followed by the evacuation of only blood or blood and mucus. The general picture is one of prostration with pallor, feeble pulse, apathy, and normal or subnormal temperature.

If examined at this early stage the abdomen is soft and relaxed; a point frequently forgotten and often leading to a delay in diagnosis. Palpation discloses in nine tenths of the cases a mass which, although most frequently encountered in the left lower quadrant, may be found almost anywhere in the abdomen. It is not uncommon to feel it on rectal examination. The absence of a mass, however, does not exclude the possibility of intussusception, for at times it may be concealed behind the liver edge in the right upper quadrant.

Once the diagnosis has been made operation should be performed immediately, the surgeon delaying only long enough to administer intravenous glucose. This step should never be omitted, since the fluids are replaced which have been lost by vomiting and the existing shock is combated at the same time. In those cases which have been neglected either from failure of the family or the physician to recognize the condition, it is a wise precaution to provide for the continued administration of fluids through a ureteral catheter inserted as a cannula in the saphenous vein. These often run for over 24 hours before clogging and may prove a lifesaving measure.

Further preoperative care should provide for the appropriate dose of morphine and atropine. Ether is usually the anesthesia of choice. During the operation measures should be taken for keeping the baby warm. One method that is quite simple is the employment of an instrument tray similar to those used in almost all operating rooms. The tray is inverted and covered with pieces of flannel and under it are placed several hot water bottles. The patient is then placed on this. Details of such a nature, although apparently trivial are important factors in reducing the mortality rate.

In those cases which are operated on during the first 24 hours after the onset of symptoms the difficulties encountered are few and reduction is relatively simple. I have found the use of white cotton gloves, drawn on over those usually worn, a great aid in handling the bowel. This permits reduction of the intussusception to be more rapidly accomplished. Sometimes the procedure takes an incredibly short time and the operator may be tempted to remove the appendix. The condition of none of these patients warrants such a step and in a long series of cases would certainly tend to raise the mortality by prolonging the operation of a patient already in shock. Most surgeons are also of the opinion that it is unnecessary to take any measures to prevent recurrence of the intussusception, as this complication is rare.

In neglected cases in which more than 24 to 36 hours have elapsed, the surgeon is often faced with a vastly more difficult problem than that of simple reduction. He may find the intussusception to be irreducible, or after reduction he may discover areas of gangrene in the bowel wall. The former condition is an unusual occurrence, according to Ladd, if the surgeon exercises reasonable perseverance in attempting reduction.

Two methods have been employed to meet such situations; resection with lateral anastomosis or resection without anastomosis, both free ends of the bowel being brought out. The mortality from each method is almost 100 per cent. Isolated cases are found in the literature in which recoveries have followed resections, but these may be considered medical rarities; for, on the whole, even in the hands of most capable men the results have been uniformly poor. Nor is it to be wondered at when we consider the age and condition of the patient, both of which prohibit the institution of such a major procedure.

During the last 2 years I have had the misfortune to be faced with such a problem and also to be present when 2 others were encountered. It was possible to effect reduction in all 3 cases, but when this had been done areas of gangrenous bowel were found near the ileocecal junction. In each instance the gangrenous portion was resected and the blind ends brought out through the wound much after the manner of Mikulicz. All 3 patients died. Our results were no different from those experienced elsewhere. In retrospect, an idea occurred to me relative to the surgical management of such cases which seemed to offer some hope of success. Occasionally, cases of intussusception have been reported in the literature which have undergone spontaneous relief of the obstruction as a result of sloughing of the invaginated portion of bowel and the expulsion of this mass per rectum. This seemed to me to offer a definite lead to a more conservative form of treatment in those cases which, following reduction, present gangrenous areas of bowel.

Montgomery and Mussil reported an experimental study of intussusception in dogs. These investigators produced an intussusception by invaginating the cecum into the ascending colon and suturing the intussusceptum to the intussusceptor at the point of invagination, to prevent its spontaneous reduction. In this fashion they were able to create a condition similar to that observed in children. After varying intervals, the dogs were reoperated on and a lateral anastomosis performed between the ileum and the transverse colon to form a short circuit around the artificially produced obstruction. In practically all the cases of their series the dogs recovered. These experiments I was able to duplicate.

The stimulus for their experimental study was excited by the results which these same investigators obtained in 2 cases of irreducible intussusception in infants in which a simple lateral anastomosis was performed around the obstruction. Both patients made a complete recovery. However, the number of cases in children in which reduction can be only partially done must be rare, since in the last 90 cases reported by Ladd this complication was not encountered. When such a condition does exist, a lateral anastomosis without resection as suggested by Montgomery and Mussil certainly affords the safest method of treatment.

From the above clinical and experimental evidence it would seem to me that we might go a step further and apply the same principles to those cases which after reduction reveal areas of gangrene of the bowel wall. These areas are almost always located within a 4-inch radius of the ileocecal valve either in the ileum or the cecum. Here, of course, where the constriction has been greatest the vascular changes in the bowel have been most pronounced.

Since the thick edematous ring at the site of origin of the invagination still persists, it would be a relatively simple matter to reproduce the intussusception far enough to cover the gangrenous portion of the bowel and to hold it here by suturing the intussusceptor to the intussusceptum to prevent its proceeding further. A lateral anastomosis could then be performed between the ileum and the transverse colon to short circuit the obstruction which has been produced. Then, if sloughing occurs in the bowel wall, it will take place within the lumen of the bowel and not into the peritoneal cavity.

The advantages of such a procedure seem to me to be as follows: first, the operation would not require as much time as resection with anastomosis or resection with the bringing out of the 2 blind ends of bowel through the abdominal incision; second, it would be less shocking to the patient; and third, the problem of fluid lost from an ileostomy would be eliminated.

In the event, however, that the patient's condition does not warrant the second step of the operation, namely, the lateral anastomosis, an ileostomy could be performed to relieve the obstruction. At some later date an anastomosis could then be attempted.

To my knowledge this procedure for treating cases of intussusception which at operation show gangrenous changes in the bowel wall has never been reported. Theoretical and experimental evidence seem to me to warrant its trial in these cases, since, when the present methods of treatment are employed, the mortality rate is almost 100 per cent.

In summary, let me reëmphasize the need of early diagnosis and the need of close coöperation between pediatrician and surgeon. The importance of preoperative administration of intravenous glucose and the maintenance of body heat during the operation cannot be overestimated. And finally, I wish to offer a method for treating those cases of intussusception with gangrenous changes in the bowel. It seems to justify its trial in view of the high mortality rate following the employment of those surgical measures now in vogue.

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HYPOGASTRIC SYMPATHECTOMY IN THE TREATMENT OF DYSMENORRHEA*

REPORT OF CASES

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Since 1889 there have appeared, occasionally, reports of presacral sympathectomy for relief of menstrual pain. In 1925 Cotte, a Frenchman, reported 200 cases with excellent results. Since then a number of articles have appeared, noteworthy among them being those of Adson and Masson of the Mayo Clinic, who reported 6 cases, and Keene of Philadelphia who recorded 7. These authors, together with several other reporters in this country, are enthusiastic about their results. I have a meager 3 cases to add to the collection.

The presacral, or more correctly, the hypogastric plexus supplies the viscera of the pelvic cavity. It is situated in front of the promontory of the sacrum, between the 2 common iliac arteries, and is formed by the union of numerous filaments, which descend on each side from the aortic plexus and from the lumbar ganglia. This plexus contains no ganglia; it bifurcates below into 2 lateral portions, which form the pelvic plexuses. It is exposed by incising the posterior peritoneum in the median line from the bifurcation of the aorta downward for a distance of 8 centimeters.

Our understanding of the sympathetic nervous system is imperfect, and clinical experience casts doubts on many current beliefs. Also, it may be difficult to explain the rationale of the relief of menstrual pain by severing the hypogastric plexus.

It is stated that the hypogastric plexus carries afferent fibers, the important pathways of sensation from the genital organs to the medullary center, and that resection of the plexus is a simple and effective way of interrupting these pathways in the treatment of dysmenorrhea. Adson and Masson, while agreeing with this view, also think that in the plexus there are efferent fibers supplying the blood vessels of the pelvic organs and that severance of these fibers is a factor in the relief of pain. The consensus of opinion seems to be that the severance of the afferent sensory fibers plays the chief rôle, vasomotor changes being secondary.

Other indications for this procedure are all painful conditions of the pelvis, especially cancer of the uterus, for which it has been used with gratifying results.

Cotte, reporting more than 200 cases, states that pain is more completely relieved when resection of the plexus is combined with other operative measures, such as uterine suspension, removal of chronically infected tubes, freeing of adhesions, etc. Also, even in patients free from such accompanying pathology presacral resection reputably has given relief.

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* Read before the Society, March 31, 1937.

In all reports in which the subject is mentioned it is stated that there has resulted no change in the rhythm of the menstrual cycle.

Cotte reported 30 normal pregnancies and normal labors subsequent to the procedure.

It is conceivable that dysfunction of the bladder and bowel might be an aftermath. In a few reports there is mention of temporary urinary incontinence.

Through the usual midline incision starting at the umbilicus the small intestine is packed off and the sigmoid pushed to the left thus giving a good exposure of the field, the landmarks of which have been described. It is said that occasionally the root of the mesocolon may extend across the interiliac space, in which instance the operation would become more difficult and hazardous. Ordinarily, however, the approach is easy, when the posterior parietal peritoneum is incised from just above the bifurcation of the aorta to just below the promontory of the sacrum. Lateral retraction of the peritoneal flaps exposes a thin sheath of fibrous tissue and fat, coursing through which can be seen the fine network of nerve fibers. By blunt dissection this sheath is lifted off the vessels and the sacrum, ligated at the upper and lower ends of the incision and excised, after which the opening in the posterior parietal peritoneum is closed.

Report of Cases

Case 1: A single woman, aged 25 years, was first seen in October, 1934. She was complaining of pain in the lower abdomen, especially at the menstrual periods, having suffered with the latter since the onset of the menstrual cycle. The appendix had been removed in 1931 and another laparotomy had been done in September, 1933. These operations failed to give relief. Vigorous treatment for 14 months by me also failed to give her relief. She came to my office 2 or 3 times weekly and at times daily. I was amazed at her persistence in accepting all that was offered her in the guise of therapeutics. I put to shame the osteopath, the chiropractor, the naturopath and last but not least the endocrinologist.

Reading Keene's article in the October, 1935, American Journal of Obstetrics and Gynecology, it took me until December to muster up courage to broach the operation to her, which I did 2 days before Christmas. She wanted it done the day after Christmas, even though I frankly told her I had never before done the operation, had never seen it done, and guaranteed nothing. I posted the operation for December 28, allowing me time to work on a cadaver in the dissecting room in the meantime.

Recovery was the same as from an uncomplicated laparotomy. The next menstrual period was January 28 to February 1, being 2 weeks late but entirely free from pain for the first time in 13 years. The menses have remained painless until the present date, 15 months later.

Case 2: A married woman, aged 30 years, mother of 1 child 8 years old, has always complained of much pain at the menstrual periods, for which I treated her with various methods at varying intervals for the last 12 years or so, with little if any success. On March 23, 1936, I performed a uterine dilatation and curettage, removed a small fibroid nodule about the size of a cherry from the posterior wall of the uterus, excised also a Morgagni cyst about one fourth inch in diameter from the left tube, and at the same time did a hypogastric sympathectomy. Since the operation her visits have been infrequent and pleasant, for she feels that she has been greatly helped. Previous to the operation she was a source of irritation to me.

Case 3: This patient was operated on on March 11, 1937, and her case is too recent to be worth while reporting in detail at this time.

Cotte, Adson and Masson, Keene, Counsellor and Craig, and others give testimony that this operation is a worth while procedure in certain well selected cases. The results in 2 of my 3 cases warrant its consideration.

I wish to forestall adverse criticism for calling this method to your attention. I do not wish to be classed as a radical enthusiast advocating this for routine use in the average case. However, once in a while one does encounter a patient who apparently suffers greatly at her menstrual periods and who in spite of our continued efforts to giver her relief continues to suffer month after month and year after year. For such a patient this operative procedure may be tried with reasonable hope for success.

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DINITROPHENOL CATARACT*

REPORT OF A CASE

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Dinitrophenol or oxy-dinitro-benzene $C_6H_3(NO_2)$ O.H. is a yellowish crystal or powder. It is used for the manufacture of azo and sulphur dyes, as a preservative of timber and in the manufacture of explosives. Dinitrophenol when taken into the body of animals can increase the consumption of oxygen to more than 10 times the normal value. The metabolism is speeded up tremendously. Horner, quoting Tainter and Cutting, notes that the increase of oxygen consumption is due to a peripheral stimulation of cellular activity. There is a decrease in the glycogen of the liver and muscles, while the sugar and lactic acid in the muscles is increased. There is evidence that not only carbohydrate but body fat is burned by the increased oxidation.

The toxic manifestations may be caused by the accumulation of oxidation products faster than they can be neutralized or eliminated by the protective mechanism of the body. The toxins thus generated manifest themselves particularly by their action on epithelial structures or those so derived. Noted are skin eruptions, in some instances to a fatal extent; severe involvement of the mucous membranes which also may be to a fatal extent; congestive infection of the middle ear; jaundice; agranulocytic angina; peripheral neuritis; abortion and damage to the liver, heart and muscles. Five deaths have been reported, of which 2 were due to malignant neutropenia. Death occurs usually within 24 hours after the onset of such toxic symptoms as vertigo, fatigue, dyspnea, high fever and excessive perspiration. Rigor mortis sets in promptly. There is no antidote. The Council on Pharmacy and Chemistry of the American Medical Association says "to treat a mild chronic condition such as obesity with a toxic agent capable of inducing serious injury and death is unjustified."

The dangers of the drug received official recognition in Germany, Canada and England in 1934. There are a large number of proprietory reducing remedies containing dinitrophenol, and very probably many cataracts have been caused by them which have been unrecognized.

Swett reports a severe case of desquamative dermatitis following the use of dinitrophenol. The mucous membranes throughout the body were involved. The patient almost died from the involvement of the gastro-intestinal mucosa. The conjunctivae sloughed. One eye was lost as a result of involvement of the cornea. The eye had to be enucleated.

Spaeth reports a case of dinitrophenol cataract with signs of tetany. He suggests that the cause of the cataract may have been a parathyroid deficiency. There was complete liquification of the lens cortex so that the nucleus was floating in a sack of fluid. Following the operation for removal of the cataract, the patient developed carpopedal spasms and there was deficient blood calcium.

In editorials in the Journal of the American Medical Association in 1933 and 1935 it was noted that poisoning by dinitrophenol during the World War was frequent among the munitions workers. Physicians and drug manufacturers have nevertheless brought about a tremendous usage of the drug. One clinic supplied to physicians and patients 1,200,000 capsules. "A drug with the potency and effects of dinitrophenol is a two-edged sword with appalling possibilities for harm as well as good." It is possible to reduce weight by limiting the intake of food, but with dinitrophenol it can be done without the imposition of self control on the individual.

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It would appear that the medical profession is at fault in this matter after the warning in these editorials which go on to say that with a drug of this potency experiments on toxicity covering several years would not be too much to demand. The possibility of hepatitis and cirrhosis should be investigated.

Nadler remarks that too much emphasis has been laid upon the possibility of dinitrophenol having an indirect or latent effect. Repeated warnings have been given particularly against its use in patients with a history of arthritis. Loss of taste and peripheral neuritis and arthritic pains have been caused. Of 22 cases reported, poisoning developed in 6. The peripheral neuritis cases showed striking sensory symptoms but no motor or trophic disturbances. It usually begins in the toes. The parasthesia persists long after the cause is removed. The delayed poisoning is due to repeated exposure to small amounts and not to an accumulation of the drug in the body.

So far as is known cataracts occur in from 0.1 to 1 per cent of those having taken dinitrophenol. The cataract may be caused by body dehydration. The cataract occurs late; some months or a year or more after taking the drug. When once the opacities appear there is rapid progress. Maturation may take place in a few weeks. Rapid swelling of the lens may cause an acute rise of intra-ocular pressure with all of its serious and destructive effects. It may produce a condition extremely difficult to deal with and which may cause loss of the eye. Such a situation may develop rapidly and without warning.

Barkan reports that all the cases seen have been in women of about the same age who had taken dinitrophenol and had lost weight. The cataracts occurred before the age of senility. They were usually bilateral and matured with great rapidity.

The anterior chamber is usually shallow due to swelling of the lens. No other deleterious effects in the eye have been noted other than the cataract. The operation for the removal of the cataracts is usually successful. The cause of the cataract formation is unknown. It may be a disturbance of the auto-oxidation system of the lens, dietary or vitamin insufficiency. In view of the alterations in and immediately beneath the capsule the cataract might be due to a change in permeability of the capsule caused by the dinitrophenol thus initiating a disturbance in the nutrition of the lens or an altered pH toward the acid side with resulting lens opacities. The delay in the formation of the cataract cannot be explained. There is marked hyperopia in some cases suggesting decrease in lens volume. It will be noted that these refractive changes are the opposite to that seen in diabetes in which myopia occurs.

Horner, Jones and Boardman first reported the formation of cataracts following the use of dinitrophenol. Since then numerous reports have been made of such catastrophes. The appearance of the cataract is characteristic. The same appearance, however, may occasionally be seen in cataract due to other causes. The first change is fine dust-like opacities just beneath the anterior capsule of the lens. They may be purely chromatic or striated. By retro-illumination the posterior capsule shows a "snow-ice" appearance with a metallic luster. One sees this frequently in beginning cataract from other causes. At this stage of the cataract the nucleus and remainder of the ocular structures remain normal.

The changes above described may affect the vision but little. The changes progress rapidly with involvement of the nucleus and the remainder of the cortex so that soon the lens is silken gray or pearly and only perception of light remains. From the time the patient first notices dimness of vision until he is quite blind may be only a few weeks. Often it is longer, several months.

Dinitrophenol has been found in the cataractous lens after its removal. A lens removed and placed in a solution of dinitrophenol shows no change. The drug injected into the aqueous and vitreous humor of the eye has no effect upon the lens. There is no data to indicate that the increased metabolism produced by dinitrophenol has a deleterious effect on the lens.

I have seen bilateral cataracts occur in a young girl who suffered severe allergic dermatitis which very closely resembled dinitrophenol cataract.

The determination of the mode of action of the drug would be of much value. If it could be safely used to hasten the maturity of a beginning cataract it would be a boon to those suffering from this condition and to the surgeon in handling such cases. In those with deterioration of vision from beginning cataract we have no satisfactory method of treatment. The intracapsular method of extraction of the cataract is unsatisfactory and dangerous in those under 50 years of age. Other methods are also unsatisfactory and not without danger.

Surgeons who have operated upon dinitrophenol cataracts are agreed that this form of cataract is relatively easily and safely operated upon. The results are usually good. Such patients have velvety black pupils and good vision promptly after operation.

Dally remarked that in France where dinitrophenol poisoning is so common, no reports of cataracts have been made. Only in the United States have cataracts occurred. He thinks it is due to an impurity in the drug, probably dinitronaphthol.

Jackson in an editorial in the American Journal of Ophthalmology says it is possible that the dinitrophenol breaks through the protective function of the lens capsule which preserves the transparency of the crystalline lens.

It is also possible that this drug poisons the subcapsular epithelium, the tissue upon which the growth and nutrition of the lens most directly depends. The drug produces marked dehydration of the body. Senile cataract seems to depend on deficiency of water taken by elderly people. Drinking freely of water may stop the progress of the opacity and in some cases definite clearing of the lens may follow. Jackson urges that if the drug is used water should be freely ingested.

It is our hope to study the action of this drug to ascertain if possible how and why it produces opacification of the crystalline lens. My colleague, Dr. Goodman, in the Department of Ophthalmology at the George Washington University School of Medicine, suggests in a personal communication that sensitization to dinitrophenol with subsequent production of a local shock reaction on the lens epithelium by injection of dinitrophenol into the anterior chamber may be a successful method of attack. This has interesting possibilities which we shall investigate.

Report of Case

Mrs. J. H. C., aged 53 years, was first seen on August 30, 1935. She had taken dinitrophenol about 2 years previously for a period of 6 weeks, dieting at the same time. She took 3 capsules a day but does not know the dosage. She lost about 35 pounds. Failing vision was first noted in the left eye in April, 1935, and in the right eye recently. The vision in the right eye with spherical +2.00 cylinder + 0.50 axis 90 was 20/30 or 91.4 per cent. The vision in the left eye with spherical +2.00 was 15/200 or approximately 24 per cent. She operated a tea room and could not see well enough to get about. The appearance of the cataract in the left eye was characteristic. Large water fissures radiated from the center of the lens and it appeared as if the lens matter was breaking up. In the right eye a faint general haze appeared throughout the lens. The tension in each eye was 19 mm. Hg. (Schiötz).

She was seen again on October 17, 1935, when the vision in the right eye was 2/200 or less than 0.1 per cent and the vision in the left eye was good for hand movements only. It will be noted that in 6 weeks the vision in the better eye had fallen from 20/30 to 2/200. This never happens in senile cataracts, whose progress is usually very slow, many years passing before the vision is reduced to the point of blindness, as had come to this poor woman in 6 months from the time she first noted failing vision. At this date, October 17, the left lens was intumescent with quite a shallow anterior chamber. Tension was 22 in each eye. Exophthalmometric readings were 26 in each eye. The left eye was exotropic.

The description of the cataracts noted on the patient's record under date of October 28, 1935, was as follows: Right eye—Throughout the cortex were a number of polyhedral shining riders, and in the center of the nucleus it seemed as if the fissures of the lens were widely separated. Left eye—The same polyhedral shining riders were seen but were less marked. In the center of the pupillary area the cortex of the lens was quite clear The nucleus showed a fissure, widely separated. I judged from this that dinitrophenol acts as a poison on the lens. With the slit lamp in the left eye could be seen an irregularly shaped grayish area directly beneath the anterior capsule in the lens, shaped like a nerve cell with its various protoplasmic processes. Throughout the part of the lens which was still clear there were a number of very fine iridescent dust-like particles, as if it were filled with metallic fragments. The riders were refractile, like crystals. The surface of the lens was grained like hammered brass or copper. The fissures in the lens were very pronounced. Obviously the lens was breaking up, much as it would after a capsulotomy. The right eye showed the condition to be the same throughout.

On October 29, 1935, the left eye was operated upon The lens acted like a mature senile cataract, except for being very mushy throughout. The cortical substance was flaky, easily washed out of the anterior chamber, leaving a perfectly black pupil. The second day after the operation the eye looked as though it had been operated on 10 days previously instead of only 2. During the convalescence a mild iritis developed which quickly cleared under appropriate treatment. There was no ascertainable cause for the iritis.

On December 6, 1935, she was given her glasses, with which she had 20/15 vision. In February, 1936, there was so much swelling of the right lens that I feared the development of secondary glaucoma. This was closely watched. The following notes were made of the condition of the lens on March 25, 1936: There is considerable intumescence of the lens with a very shallow anterior chamber. The nucleus of the lens is breaking up much as it would after a needling, but the anterior cortex is still clear. In May, 1936, the ophthalmoscopic examination showed no iris shadow on the front of the lens. The nucleus was opaque and had undergone division. This separation was caused by a large 3-pronged water fissure. The anterior cortex substance was relatively clear but had a number of pearly areas in it. There was considerable intumescence, and because of this and the disintegration of the nucleus it was thought best to remove the lens. On June 2, 1936, the right eye was operated on, with subsequent uneventful recovery and restoration to normal vision.

From the descriptions of others this was a typical cataract produced by dinitrophenol.

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The Clinical and Pathological Features of Tumors Occurring in the Region of the Apex of the Lung.—. . . Not until 1924, and again in 1932, when Pancoast described a series of cases under the title of "Superior Pulmonary Sulcus Tumors," was proper attention directed to the region of the apex of the lung. The above term was given by him "because this term implies its approximate location and a lack of origin from the lung, pleura, ribs or mediastinum." However, he wisely stated that "it is possible that this new designation may be changed again with a better knowledge of the histopathology of the growth."

His criteria for the diagnosis of tumors in the above group were as follows: pain around the shoulder and down the inner side of the forearm, Horner's syndrome and evidence of wasting of the muscles of the hand with subsequent loss of strength. The roentgenographic appearance showed a small circumscribed shadow in the apex of the lung due to lung displacement, destruction of the posterior portions of one or more ribs and also possible involvement of the posterior parts of the transverse processes or sides of the bodies of the vertebrae. Intrathoracic metastasis was not present. He concluded that the tumor as a distinct entity might take its origin in an embryonal epithelial rest and that primary lung tumor could be ruled out.

Although tumors other than those arising from the terminal bronchioles in the lung will fulfil all the criteria of the clinical entity described by Pancoast as superior pulmonary sulcus tumors, those arising in the lung are the most common. In the great majority of cases, the superior pulmonary sulcus tumor is really an atypical form of primary carcinoma of the bronchus, and when Horner's syndrome and symptoms of brachial plexus compression are encountered, this type of tumor should be suspected.

Eight cases fulfilling the requirements given by Pancoast are described. . . .

Discussion. . . . I am of the same opinion as Browder and Deveer, namely, that malignant tumors occurring in the region of the pulmonary apex may produce the symptoms and findings described by Pancoast solely because of their anatomical location and not because of a specific pathological structure. However, since 1838, when Hare probably reported the first so-called superior pulmonary sulcus tumor (but not by any specific name) 44 cases have been reported in the literature, the majority of which have been carcinomas of the lung.

A differential diagnosis in cases presenting symptoms produced by invasion of, or pressure on, the brachial plexus, erosion of ribs or vertebrae and sympathetic nerve changes, must include cervical tumors, aneurism, apical tuberculosis, cervical ribs, primary lung tumors and metastatic lesions to the pulmonary apex.

Conclusions.—1. The majority of malignant tumors located in the region of the superior pulmonary sulcus are carcinomas of the terminal bronchioles of the lung.

2. The diagnosis of superior pulmonary sulcus tumor is not entirely adequate unless qualified as to whether it is a primary or metastatic lesion.

3. Patients complaining of pain around the shoulder radiating down the inner side of the forearm, Horner's syndrome and wasting and weakness of the muscles of the forearm and hand, should be suspected of having a tumor in the region of the apex of the lung.

4. Irradiation is of no less value in these cases than in the cases of carcinoma of the bronchus generally seen.

Abstract from article by Justin J. Stein, M.D., Hines Illinois, *Texas State Journal of Medicine, August, 1937, p. 293.*

EVALUATION OF MEDICAL THERAPY OF THE UPPER GASTRO-INTESTINAL TRACT*

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When Prometheus stole the Olympian fire for mankind, I believe he must have slipped in some stomach remedy with it. If we glance through the writings of all ages, we find a multitude of references to stomach ailments and their medications. Indeed, the epigrams of Martial, Rabelais and Shakespeare would lose their saucy flavor without the quips about the "bellyache." The stomach undoubtedly was, is and will be the most universally abused organ in the body. Instead of the tender loving care to which it is entitled, it is treated like the worst pariah.

The stomach, however, is magnanimous, for even though it may be abused for a long period of time, when given proper sympathetic attention its functions return, maybe meekly, maybe not like the flaming youth it used to be, nevertheless with some semblance of the return to normal function either in motile or secretory sphere.

In using medications for the upper intestinal tract, it is imperative to know their proven optimal actions and conditions under which they exert their beneficial effect. I have undertaken to evaluate only these therapeutic agents which are most commonly used and abused.

Alkalies have been widely advertised as a panacea for "what ails you" in the stomach (Bastedo; Kantor; Johnson and Henderson; Jeghers and Lerner). Proprietary alkalies, such as, Cal-bis-ma, Alkazene, Soda Mints, etcetera, are only too well known. Ordinarily they are used in the "alkali" treatment for peptic ulcer, "hyperacidity," heart burn and "hangover." I shall not discuss whether the "alkali" treatment of peptic ulcer is more rational than other methods, but I want to mention that it is predicated upon the theory that it neutralizes hydrochloric acid and abolishes the "hunger pain" or "empty pain" or whatever you call this gnawing sensation occurring at the height of digestion 3 to 4 hours after partaking a meal.

The cause of hunger pain, alas, is not as yet known, in spite of extensive research work, and it is paradoxical that an irritant such as peppermint will relieve this pain similarly to the action of sodium bicarbonate, an alkali. So far as the action of alkalies goes in neutralizing hyperacidity, whether associated with an ulcer or without it, it is at best a temporary measure. When the gastric parietal glands have a definite secretory hydrochloric acid level and the acid present is neutralized by an alkali, as soon as the neutralization occurs the glands begin to work overtime to catch up with their normal hydrochloric acid level. If one continues to pour in alkalies, these glands finally become exhausted and a temporary or permanent suppression of hydrochloric acid occurs. This is number 1 danger in alkali therapy. The second one is that the acid ions in the stomach are of a certain definite strength, and if they are overwhelmed by excessively strong basic ions there will result an impairment of the acid-base regulating mechanism of the body. Therefore, in medicating with alkalies, one must know the ability of the body to utilize basic ions. To do so, blood chlorides and nonprotein nitrogen estimation should be made often, since at the first sign of alkalosis there is a definite drop in the chlorides and rise in the nitrogen of the blood. It is important to remember that any other impairment of the body, such as renal disease, cardiac ailment or asthma will decrease the body's abilities to utilize alkalies. Therefore, one should bear in mind the early signs of alkalosis, such as distaste for milk, abdominal pain, nausea, vomiting, dizziness, occipital headaches. The best alkalies to use are those which possess the weakest base ions, namely, tribasic calcium, magnesium phosphate and colloidal aluminum oxides. The calcium salts being constipating can be used in cases of hyperacidity accompanied by diarrhea. The magnesium salt may be used in cases of hyperacidity when there is a tendency to constipation.

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* Read before the Section on Internal Medicine, March 27, 1937.

Antispasmodics, atropine and belladonna have gained great popularity in recent years. These drugs were used in spasm of the gastro-intestinal tube, in gastric hyper-secretion and finally routinely on every patient who came with a stomach complaint. To Bastedo goes the credit for breaking down this fatalistic belief in the atropine group. He has established the fact that if you do get a satisfactory result from belladonna or atropine medication, it must be given in doses to give signs of toxicity, such as irritability, pupillary dilatation and dryness of the throat. The usual minimal dose to do so is 1 milligram of atropine by hypodermic injection or 45 minims of standard fresh tincture of belladonna preparation, used ½ hour before meals Certain susceptible individuals require smaller dosage.

Belladonna has a limited value in gastro-intestinal therapy. Its uses should be restricted when there is interprandial hyperacidity because of the associated danger that although it decreases interprandial hyperacidity, at the same time it increases the digestive hyperacidity, a thing physiologically not wanted. Its second action is that it reduces spasm of the intestinal tube, such as pylorospasm, but the measure is very temporary and not constant. In certain cases it may even increase the spasm, especially the one due to tobacco irritation and emotional instability.

Kendall of New York has written about Novatropine in therapy of the gastro-intestinal tract, claiming its action similar to atropine but without its toxic effect. I regret to state that my experience with belladonna derivatives did not justify the therapeutic claim of the authors. Using them, there were no toxic side effects but there were also no therapeutic benefits.

The best antispasmodic today for short action, I may state, is benzedrine sulphate (Myerson and Ritvo). It is used orally in total dosage of from 30 to 40 milligrams daily. It should be given in 10 mg. doses 3 times a day, 3 hours after each main meal (at the height of digestion). Its effect is almost immediate and the majority of patients have no discomfiture. Few will complain of slight restlessness, general ache and diarrhea. Alas, it has very little effect upon the lower segments, such as the sigmoid or rectum, and therefore it is useless in spastic constipation.

Gastric hypermotility is affected by ephedrine sulphate, 1 grain per day; this prolongs the emptying time by about 90 per cent (Van Liere, et al.). This should be borne in mind, so that in cases of gastric retention the physician will investigate whether or not the patient suffers from asthma or urticaria and takes ephedrine regularly, which may be the cause of the retention.

For malnutrition bitters are useful, since they promote appetite; but in congenital cachexia, in which the appetite is normal, they are of no use. They also promote secretion of gastric juice in subacidity. Bitters should be administered about 15 minutes before meals in just a sufficient dose to give a strong bitter taste, but not large enough to act as a depressant to the stomach. Usage of alcoholic beverages in malnutrition, such as eggnog, sherry or champagne received a blow by the recent investigation of Blotner of Boston. He showed that a proper amount of alcohol destroys the proteolytic activity of gastric juice, trypsin and pancreatin in vitro and in vivo. To prove it, he used a 48 per cent alcohol solution. Naturally, alcohol in such high concentration will act as an irritant to the gastric mucosa and a depressant to its secretions.

The alcoholic beverage to be used in malnutrition should not exceed 8 to 10 per cent of alcohol. Natural, fermenting wines possess that strength. The expensive wines advertised as having 20 to 30 per cent alcohol are not simple wines but fortified wines, and should not be used. Therefore, if we order sherry or table wines for these patients, the strength must not exceed 10 per cent of alcohol if beneficial results with therapeutic actions similar to the bitters are to be obtained.

Tobacco, although not a therapeutic measure, should be discussed, because of the extensive campaign of certain tobacco manufacturers who claim that smoking aids digestion. The facts are that tobacco increases the secretion of hydrochloric acid at first and when used extensively and for a long period of time finally causes a suppression of it. It also destroys the proteolytic activity of the gastric enzymes, and that is why in cases of malnutrition, in which the patient is also a smoker, no medication such as a high caloric diet, insulin, change of environment, or rest will be of avail unless tobacco is withdrawn. It acts as an irritant to the gastro-intestinal mucosa, causing hypermotility, and it should therefore also be withdrawn in medication of a diseased gastro-intestinal lining, ulcer or pylorospasm (Barnett). The minor beneficial effect it has is a soothing effect upon the nervous system and only when used in small amounts.

In conclusion, I wish to state that I have limited myself to the discussion of few of the medical therapeutic agents and problems, especially the ones which seemed to me as being physiologically misused, since the field of medical therapy of the gastro-intestinal tract is too large to cover in one short paper. I shall conclude with an old Roman maxim: "*Graviora quedam sunt remedia periculis*"—Some remedies are worse than the disease.

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Regional Enteritis; Report of Five Cases.—In 1932 Crohn, Ginzburg, and Oppenheimer reported 14 cases of what they considered a distinct clinical and pathological entity of the ileum. They considered their cases as separate from the group of so-called "benign granulomas" previously reported in the medical literature. The latter constituted all chronic inflammatory lesions of both the large and small intestine whose etiology was unknown. At present there exists some difference of opinion whether or not the type of lesion described by Crohn and his associates may be considered as apart from the other lesions of this group. It has been shown that the term ileitis used by these authors is incorrect, since an identical pathological process occurs in other parts of the small intestine. Moreover, in a recent article these authors have admitted that their original conception of the location of the disease as occurring only in the ileum was incorrect and they now believe it may even involve the large bowel.

Regardless of whether Crohn and his workers are correct in their contentions, they have made a distinct contribution to medical science by focusing attention to this often-overlooked disease. They have so popularized the subject that within a period of 5 years over 200 cases have been reported in the American literature.

The question has been asked: Is this disease actually a new clinical entity, or is it one that has merely escaped the eyes of the roentgenologist, clinicians, pathologists and surgeons? While X-ray studies and physical examinations might not have shown the disease in years gone by, it could hardly have failed detection at the operating table or at postmortem examination. In fact one of the cases in this series was resected by my brother Reginald, 27 years ago and again in 1927. We encountered a very extensive case involving the duodenum and jejunum. This entire segment of bowel appeared like a thick, rubber hose, and due to the great extent of the lesion and because so little was known concerning the disease, resection was considered inadvisable. This patient died within a year. In light of more recent knowledge, we now recognize this case as one, perhaps, best termed regional enteritis. . . .

Conclusion. . . . I should like to emphasize the following points:

While regional enteritis was recognized as a distinct entity but 5 years ago, there have now been reported 219 cases in this country.

Although its etiology is obscure, early recognition with proper surgical measures results in prompt relief of symptoms and probable cure.

The signs and symptoms may closely simulate acute appendicitis, ulcerative colitis, partial intestinal obstruction, and ileocecal tuberculosis depending upon the stage of the disease.

The majority of cases reported have previously had appendectomy performed with failure to relieve symptoms. This emphasizes the importance of a careful diagnosis in every abdominal case coming to surgery and imposes upon the surgeon the necessity of a thorough abdominal exploration when conditions so indicate.

Roentgenological findings are characteristic and an invaluable aid to diagnosis.

The type of operation to be performed depends upon the individual case. . . .

Abstract from Case Reports by Arnold S. Jackson M.D., Madison, *The Wisconsin Medical Journal, August, 1937, p. 632.*

BONE-MARROW FINDINGS IN THE DIAGNOSIS OF CERTAIN BLOOD DYSCRASIAS*

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Despite the fact that many different types of cells are found in the circulating blood and despite the fact, also, that changes in these cells are the immediate cause of symptoms which arise in the blood dyscrasias, none of the cells arises in the circulation, but rather is formed at an entirely different location. In this respect cells of the hemopoietic tissues are unique; there is no other organ or tissue which forms cells, the usual product of activity being a secretion usually of a chemically distinct substance, such as thyroxin from the thyroid or insulin from the pancreas.

This unique feature of the bone marrow, namely, that it produces cells of different types for circulation in the blood, has however been responsible for a considerable amount of confusion in the study of its diseases. In the past, for instance, it has been believed that by examination of the cells which were present in the circulating blood, one could tell what was the condition of affairs in the tissues producing these cells. In many instances one may come remarkably close to forecasting what kind of disturbance has taken place within the bone marrow, but in many instances also the forecast is very erroneous.

Probably this fact has been recognized before to judge by previous attempts to study the bone marrow, but regardless of these few efforts the bone marrow seems rather well to have escaped study. Encasement of the marrow tissue within the bony covering of the ribs, vertebrae and long bones seems to have been the reason why such studies never received the attention due them. Ghedini apparently was the first to study the bone marrow in man. Following this, a series of papers appeared at intervals until Peabody's classic paper in 1927. Peabody, in common with many who preceded him, utilized the bone marrow obtained by tibial biopsy. Custer and Dameshek have studied bone marrow obtained by removal of buttons of bone from the sternum. More recently Osgood and many other workers have utilized a different technic for obtaining the material. The site selected has been the sternum, and the means by which its contents were obtained was aspiration by a needle with a syringe. Just as in the earlier method there was the objection that the procedure was a rather formidable operation, so in this later method there is the objection that the material aspirated consists chiefly of venous blood with a few bone marrow cells scattered throughout. The methods at hand thus are rather complicated from the standpoint of thorough clinical study of patients with disturbances in blood-cell formation.

It seemed evident that if a trephine of sufficiently small caliber could be used, the procedure might become a most useful and widely used one. Not only would it be possible to carry out the studies readily and accurately but also it would be possible to repeat the studies after relatively brief intervals. This latter advantage would permit study of the response to medication at relatively frequent intervals.

The procedure used in the present studies (Weller) consists in insertion of an 18-gauge spinal needle with stylet in place cephalward into the sternum at the angle of Louis. With 5 per cent novocain infiltration the patient feels only a sense of pressure until the needle has penetrated the outer layer of cortical bone. Once the tip of the needle is within the marrow no discomfort is felt unless the needle is twisted, when sharp pain results. After the cortical layer of bone has been penetrated, the stylet is removed and the needle pushed forward a distance of 5 to 10 mm.; then it is removed slowly, and the material within the lumen is spread out in a thin film on a glass slide.

Practically all of the patients included in the present study have one point in common, namely, the presence of an anemia. For purposes of comparison, however, a knowledge of the sternal marrow from a normal individual is first necessary. In these circumstances the bone marrow in the gross is grayish-yellow and gelatinous. When spread upon the slide a moderate amount of fat collects in droplets. The stained film shows a definite architecture of a network of cells infiltrated with fat globules.

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* Read before the Society, November 18, 1936.

The cells which constitute this network are about evenly divided between the red-cell and white-cell series. In general the numbers of each are few, but the grouping is fairly constant as one proceeds from area to area in the film. The cells of the erythrocyte series usually are erythroblasts or normoblasts, only an occasional megaloblast being seen for the most part. The cells of the leukocyte series are myelocytes, only an occasional myeloblast being seen. In addition eosinophils and basophils as well as an occasional megakaryocyte are to be found.

In the case of anemia secondary to carcinoma of the stomach, for instance, the architecture resembles to a moderate degree that of the normal sternal marrow architecture. The difference consists chiefly in the increased size of the fat droplets, and the fact that in the reticulum there is a smaller number of cells of both the red-cell and white-cell series.

In the case of the classic type of pernicious anemia an entirely different state of affairs exists. The bone marrow is very hyperplastic, all semblances of architecture have disappeared in the films, and one finds large numbers of megaloblasts. The polymorphonuclear cells which are present in the advanced stage of untreated pernicious anemia are for the most part very mature, and the number exceeds that of the myelocytes. After treatment with potent liver extract the picture changes considerably and this is the time when semblances of the normal architecture begin to be seen depending upon the stage to which the treatment has been carried.

In the case of myeloid leukemia the sternal marrow again is very hyperplastic. The cells are mainly of the myeloid series with mature polymorphonuclear cells, myelocytes and myeloblasts as well as eosinophils predominating. The number of eosinophil cells is definitely increased above normal in this type of disturbance.

In general, insofar as cases of pernicious anemia are concerned, the changes which have been observed in the bone-marrow cells by this method coincide with those described by previous observers. Despite the fact that Peabody utilized biopsies of the tibial rather than sternal bone marrow, the present studies agree with his findings in that the change is particularly in the immaturity of the cell forms which are present.

As regards pernicious anemia in colored persons the present studies indicate that this condition is not particularly rare, certainly not as rare as one is led to believe from the literature. The changes in these patients also follow the previously described changes in the bone marrow which have been accepted as characteristic of pernicious anemia.

Thus far no case of aleukemic leukemia has been observed. Several patients with relatively low leukocyte counts have been studied, however, and it has been found that the bone marrow in these cases is practically identical from the cytological standpoint, with the bone marrow in pernicious anemia. This, it is believed, is corroboration of the excellent clinical results obtained by Murphy in the treatment of so called "agranulocytosis" by intramuscular injections of liver extract. In the cases with low leukocyte counts the presence of free hydrochloric acid in the gastric contents seems no obstacle to the administration of liver extract.

Of the 2 cases of myeloid leukemia in which simultaneous studies of both peripheral blood and bone marrow have been carried out, it was found in 1 that the changes in cells in the circulating blood were relatively slight, while the bone-marrow biopsy specimens showed marked abnormalities.

In the present series of cases, 2 have satisfied the criteria for aplastic anemia, that is, there was no response to any form of medication. In these cases the bone-marrow specimens showed a certain number of stem cells present, the total number, however, being far below that found in an untreated case of pernicious anemia with an erythrocyte count at a corresponding level.

In summary, the greatest help to be obtained from sternal marrow biopsies is information concerning the direction which therapeutic management of the case should take. Regardless of certain unusual cells in the circulating blood, or the presence of free hydrochloric acid in the stomach contents, if there is a megaloblastic hyperplasia of the bone marrow cells then liver extract is indicated. If the stem cells are few in number, little response to therapeutic measures is to be expected. If, finally, the bone-marrow cells are abnormal in kinds and numbers, even though those in the circulating blood are relatively normal, the case deserves diagnosis and management as one of the neoplastic diseases (leukemia).

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ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"Petrous Apex Empyema. Some Remarks on Its Management,"* **Mervin C. Myerson, M.D.**, New York City.

Infection of the petrous pyramid occurs approximately once in every 300 cases of otitis media. This condition either resolves spontaneously, extends by means of the vascular channels to terminate in a fatal meningitis, or localizes, usually in the apex area as an empyema. The group of empyemas can be cured by surgical measures.

A definite plan for the surgical management of localized petrous apex suppuration is suggested. In this plan we should adhere as closely as possible to conservative measures. By conservative measures we mean the avoidance of radical mastoidectomy and the elimination, if possible, of extensive and mutilating surgery such as is advocated in the Ramadier or Lempert operation.

One may differentiate by means of X-ray studies 2 locations of the infection, a superior and an inferior. In the superiorly located infection the line of the roof of the apex cavity is absent on the film taken in the Stenver or supero-inferior position. In the inferiorly placed infection the line of the roof is intact on this film, but there is loss of definition of the bony structure of the petrous apex on the film taken in the base of mento-vertical position.

The surgical attack is planned according to whether the disease is located superiorly or inferiorly in the apex. It is at once apparent that a surgical approach from above would not accomplish drainage of the empyema in the inferiorly placed infection. A softened tract of bone may exist below the posterior semicircular canal through which the apex area could be entered by means of a probing instrument, and the pus evacuated. If this cannot be accomplished and there is no evidence of beginning spread to the cerebellar dura, the otologist may wait for the pus to burrow through the inferior wall of the petrous apex and cause a high nasopharyngeal abscess. This occurs in a great majority of such cases. When this is so the abscess either ruptures spontaneously or requires incision. If, however, there is evidence of beginning spread to the meninges or to structures other than the retropharyngeal space, the cervical operation for attacking the inferior aspect of the petrous apex should be done. This will insure drainage and prevent serious complications.

In the superiorly placed infections a softened tract of bone leading into the apex should be sought in one of the following locations: Anterior to the superior semicircular canal; above the arch of the superior semicircular canal; in the arch of the superior semicircular canal; posterior to the superior semicircular canal; posterior to the posterior semicircular canal; inferior to the posterior semicircular canal.

The apex empyema can be evacuated through such a tract of softened bone, and all these areas can be exposed and probed by means of the exposure afforded by a simple mastoidectomy. In many bones the tegmen of the mastoid must be removed down to the superior semicircular canal so as to afford easier access to these structures.

If a softened tract of bone leading into the apex is not discovered, the apex should be exposed by elevating the temporal lobe. In order to accomplish this a large area of the squama is removed. The area of removal extends from the region of the sino dural angle to about one half inch anterior to the root of the zygoma and is approximately the size of a silver dollar. The elevation of the temporal lobe down to the uncapped tip area is met with a gush of pus.

There is no necessity for destroying the middle ear structures and causing deafness by performing a radical mastoidectomy, nor is it necessary to injure the temporomandibular joint as is done in the operation of Ramadier and Lempert.

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* Presented at the joint meeting of the Section on Ophthalmology and Otolaryngology and the Society, April 16, 1937.

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WHITHER REGIMENTATION

Regimentation, a word which is anathema to the medical profession because of its implications is heard oft repeated. If it were not for attempts open and veiled to put it in practice, the word and its meaning would soon cease to stir the emotions and cause activity of the combined profession's thought. It suggests loss of that individuality which has brought discoveries of infinite benefit to the afflicted and the widespread distribution of medical care to the needy in dispensaries, hospitals and in private homes. It surely suggests acceptance of commands with immediate obedience. Commands from what source? Obedience to whom? Ah, there is something to conjure with. The designating of "a certain class of doctors by the President or by some officers of the Federal government who then become a board who are to pass on their fellow-doctors' having the right to be admitted to be practitioners under the federal law," is included in a plan recently proposed. The federal licensing of physicians! Again there are in evidence plans for the placing of the doctor on a salary, working full time. He would take his orders from some political appointee, i.e., if he happens to be serving a medical service group under national or state control. The matter of diagnosis and treatment, dictated by high command; hours and wages for this labor also dictated. Proposals of all sorts are abroad in the land to line up physicians in "formations as in a regiment."* The threats of forceful organizing by politicians outside of the ranks with political plums in boards and directorates is what the profession seriously objects to. The sophistry in handling statistics, which is often apparent, should be exposed, i.e., it believes that only by distortion of evidence can it be claimed there is wide-spread lack of opportunity of the populace to obtain adequate medical care. Doubts arise as to the imposed leadership having the caliber to give that part of humanity afflicted with disease a square deal. The threat of politics, the failure of the sick to have free choice of physician, seem inseparately connoted in the term regimentation.

NEWS AND PERSONALS

The Second Annual Alumni Extension Course of the Georgetown University School of Medicine will be held this year, September 13 to 17, inclusive. There will be general sessions of interest to all and clinics in various branches of medicine and the specialties for those interested in the different fields of medical and surgical practice. The general sessions will include lectures on topics concerning recent advances of various kinds, delivered by members of the faculty and by prominent guest speakers, and medical movies. Special ward rounds and clinical demonstrations not included in the printed program will be arranged if requested.

Medicine.—In the field of internal medicine such subjects will be considered as the use of prontylin and prontosil for various infections; the use of ergotamine tartrate for migraine; the use of benzedrine sulphate for exhaustion, pylorospasm and other purposes; the use of protamine zinc insulin; the pharmacology and therapeutics of the barbiturates; iontophoresis with mecholyl preparations for chronic ulcers; the diagnosis of vitamin C deficiency and its treatment; rapid typing in pneumonia; the treatment of pneumonia; gastroscopy; unusual forms of hypertension; the surgical treatment of hypertension; motion-pictures on endocrinology; various blood dyscrasias; the treatment of gastric neuroses; the diagnosis of liver disease; gouty arthritis. Guest speakers will include Dr. Maurice C. Pincoffs, Professor of Medicine of the University of Maryland; Dr. Irving S. Wright of the New York Post-Graduate Hospital; Dr. Irvine H. Page of the Rockefeller Institute of New York; and Dr. Sanford M. Rosenthal of the National Institute of Health.

Surgery and Allied Specialties.—There will be Operative Surgical Clinics on Tuesday and Thursday at the Georgetown University Hospital. This schedule will be supplemented by other clinics by members of the Surgical Department at both Gallinger Municipal and Providence Hospitals. It is the intention of the Surgical Service to provide clinics daily for those who will be interested. There will also be surgical motion-pictures. These pictures are most instructive and will be the identical films which have been shown at the recent Clinical Congress of the American College of Surgeons. There will also be special or alternate courses for those interested in orthopedic surgery; proctology; genito-urinary surgery; neurosurgery; ear, nose and throat, including bronchoscopy; ophthalmology; and radiology.

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* Definition of regimentation in New Standard Dictionary.

Obstetrics and Gynecology.—The outstanding feature of the course in obstetrics and gynecology will be an address by the distinguished gynecologist, Dr. Emil Novak of Baltimore, who will discuss "Endocrinology as Related to Obstetrics and Gynecology" at one of the general sessions. In addition, there will be one afternoon devoted to obstetrics, when recent advances will be presented by various members of the department. Noteworthy will be the report of a study of pregnandial as a pregnancy test. It is hoped also to have an obstetrical operative clinic one morning at Gallinger Municipal Hospital. Of course, such a clinic is always problematical, but with Gallinger Municipal Hospital's large obstetrical service of about 2,400 deliveries annually it is more than likely that some cases can be presented. Gynecological operative clinics will be held on two mornings at the Georgetown University Hospital and possibly at other hospitals.

Pediatrics.—The course in pediatrics will embrace modern methods of simplified infant feeding, together with the consideration of recent treatment of diseases affecting infants and children. Advances in the treatment of genito-urinary diseases, including vulvovaginitis and pyuria, will be demonstrated by the pediatric staff in association with pediatric urologists. The value and technic of preventive immunizations in childhood and the practical application of such measures in the practice of medicine will be considered.

Pathology.—Clinicopathologic conferences will be held.

Psychiatry.—One hour will be devoted to the subject of modern trends in psychiatry.

Golf Tournament.—As a period of recreation during the strenuous week, a golf tournament will be held on the splendid links of the Georgetown Preparatory School on Thursday afternoon, September 17.

Alumni Banquet.—A Shore Dinner with entertainment and dancing will be served on Friday evening, September 17, for alumni and their ladies.

Georgetown University School of Medicine. *Changes in Faculty Appointments, Effective September 1, 1937.*

Dr. Vincent J. Dardinski, formerly professor of anatomy, is to become full-time pathologist and director of the laboratories of the University Hospital.

Dr. John R. Cavanagh, associate clinical professor of medicine, will take the position of director of the Outpatient Department of the University Hospital.

Dr. Frank S. Horvath, associate clinical professor of medicine, will become assistant director of the Outpatient Department of the University Hospital and supervisor of student instruction in the Outpatient Department.

Section on Ophthalmology and Otolaryngology organized for the coming year, as follows:

Earle G. Breeding, *Chairman*
Richard A. Kearny, *Vice Chairman*
Elmer R. Shepherd, *Secretary*
John H. Trinder, *Treasurer*
James A. Flynn, A. B. Bennett, E. J. Cummings } *Executive Committee*

Section on Gastro-enterology is Organized. At a meeting, held on the evening of May 28, plans for the organization of a new Section of the Medical Society of the District of Columbia were formulated. It has been arranged to hold meetings on the second Monday of alternate months, beginning with October and extending through June. The tentative officers are: Drs. Matthew White Ferry, *Chairman;* Fred A. J. Geier, *Vice Chairman;* Roy Lyman Sexton, *Secretary-Treasurer.* The following were present at the initial meeting:

Drs. Leo T. Brown, William F. Burdick, William Earl Clark, Sidney C. Cousins, Richard E. Dunkley, Fred A. J. Geier, William T. Gill, Jr., Clapham P. King, Alan Frank Kreglow, Janvier W. Lindsay, James Alexander Lyon, William J. Mallory, R. Sterling McGrath, W. Ross Morris, L. B Norris, Matthew White Perry, John A. Reed, Antoine Schneider, Henry R. Schreiber, R. Lyman Sexton, A. Camp Stanley and J. Russell Verbrycke, Jr.

The Aesculapian Society is one of the newly organized smaller societies with limited membership that has not been noted in the Annals. The objectives include "presentation and discussion of scientific papers of interest to the medical profession." The present officers are: Drs. Raymond C. Kirchner, *President*; Frank R. Shea, *Secretary-Treasurer.* Meetings are held on the first Tuesday of each calendar month in Suite 207, 1726 Eye Street, N.W.

Washington Medical and Surgical Society announces the election of officers for 1937–1938, as follows: Drs. Joseph Horgan, *President;* Robert Oden, *Vice President;* Beveridge Miller, *Secretary;* Frank E. Gibson, *Permanent Treasurer.*

American Medical Association Addresses Broadcasts through the facilities of the National Broadcasting Company, 1937–1938, "To America's

Schools—Your Health." The programs, which may be obtained in advance in "Hygeia," the Association's health magazine, will be planned especially for junior and senior high schools; designed in assisting health teachers in illustrating, amplifying and enriching their courses of instruction to adolescent children. The accompanying musical theme, "Hail and Hearty," written especially for the program, will add materially in emphasis and enjoyment.

Association of Military Surgeons of the United States will hold its 45th Annual Convention at the Ambassador Hotel, Los Angeles, October 14–16, 1937. The program will include such subjects as "Fleet Medicine," "Eyes in Aviation," "Ears in Aviation," "The Training of Medical Officers in a Major War Emergency," "Physiotherapy in the Next War," "Modern Typhoid Treatment," "Hospital Ships in the World War: Lessons to be Learned from Them," "Anesthesia in Shock," "Submarine Medicine," "Emergency Plastic Surgery," and "The Blood Sedimentation Rate in Dental Infections." The Presidental Address will be given by Rear Admiral P. S. Rossiter, Surgeon General of the United States Navy. Colonel Howard Naffziger, Medical Reserves, United States Army, will be the guest speaker—subject, "Surgical Treatment of Low Back Pain."

Academy of Physical Medicine meets October 19–21, 1937, in Philadelphia, Pa. Demonstration clinics will be held at the hospitals of the University of Pennsylvania, Jefferson Medical College, and Temple University. The Academy is international in scope. Program may be obtained by addressing Dr William D. McFee, Chairman, Committee on Program and Publication, 41 Bay State Road, Boston, Mass.

Dr. John B. Nichols, a former President of the Medical Society (1912), member of the Society's Medical Defense Committee since 1928, was honored upon his completing 35 years of service as Medical Director of the Acacia Mutual Life Insurance Company at an informal meeting of officers and staff members. Dr. Nichols' seniority number is 232.

Mr. Frederick A. Fenning, an Honorary Member of this Society, also the Society's Counsel, read a paper on the evening of July 30, 1937, before the Hancock County Medical Society at Bar Harbor, Maine, on the subject, "Medical Jurisprudence." Appearing on the same program was Dr. Fritz B. Talbot, Harvard University School of Medicine.

REPRINTS RECEIVED

The following reprints have recently been received for which due acknowledgment is made:

"Nondrainage of the Peritoneal Cavity in Appendiceal Peritonitis," Edward A. Cafritz, M.D., Journal, American Medical Association, April 17, 1937.

"A Case of Lipophagic Granuloma and Scleroma Neonatorum," F. J. Eichenlaub, M.D., and I. Lewis Sandler, M.D., Southern Medical Journal, May, 1937.

"An Experimental Study of Injuries of the Kidney," W. Calhoun Stirling, M.D., and A. M. Lands, Ph.D., Journal of Urology, April, 1937.

"Preventive Immunizations in Childhood," Joseph S. Wall, M.D., Archives of Pediatrics, April, 1937.

CONTAGIOUS DISEASE REPORTS

Health Department, District of Columbia

June, 1937

	Mortality	*Morbidity*
Typhoid fever	10	0
Typhus fever	0	0
Smallpox	0	0
Measles	358	4
Scarlet fever	27	0
Whooping cough	79	5
Diphtheria	54	2
Influenza	1	1
Poliomyelitis	0	0
Encephalitis-lethargica	0	0
Epidemic cerebrospinal meningitis	9	4
Tuberculosis (all forms)	116	53
Syphilis	511	8
Chancroid	7	0
Gonorrhea	319	0
Chickenpox	94	0
Pellagra	0	0
Pneumonia (all forms)	35	24
Typhoid fever	17	2
Typhus fever	0	0
Smallpox	0	0
Measles	109	0
Scarlet fever	14	0
Whooping cough	46	1
Diphtheria	29	0
Influenza	0	0
Poliomyelitis	1	0
Encephalitis-lethargica	1	1
Epidemic cerebrospinal meningitis	0	0
Tuberculosis (all forms)	155	45
Syphilis	481	8
Chancroid	2	0
Gonorrhea	346	1
Chickenpox	18	0
Pellagra	2	2
Pneumonia (all forms)	29	31

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PHYSIOLOGICAL RESPONSE TO MASSIVE INFUSIONS OF PHYSIOLOGICAL SALT SOLUTION*

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The normal way of taking food and drink into the body is by mouth. Unless there is some good reason to the contrary this is the manner in which food and drink should be administered to the patient as well as to the healthy person. When, under abnormal conditions, the intestinal tract grossly fails to function as it should, and particularly when stomach and intestine reject anything and everything that is presented to them, this normal avenue of nutrition is closed. Under such circumstances, although malnutrition and starvation loom as ultimate possibilities, the immediate cause for concern is lack of water—dehydration, which unless relieved closes the scene much more promptly than is frequently appreciated.

Of the various possible parenteral methods for the administration of food and water the intravenous route is the most direct; for this reason, other things being equal, it would seem to be the most desirable. Unfortunately, the evidence that intravenous infusions are safe and particularly the evidence that they are entirely rational is not all that could be desired. Many a conscientious physician probably hesitates to use so direct a method because he is not satisfied that by so doing he places no undue strain on the circulation, does no damage to the acid-base balance of the blood, imposes no ultimate burden on the liver or kidneys, or otherwise subjects his patient to unnecessary hazards.

The two questions which need to be answered before intravenous infusion can become an entirely trustworthy method are: Do we accomplish precisely the same ends when we give glucose, or salt, or water by vein as when we feed these same substances by mouth? How large doses are physiological and how rapidly may they be administered with entire safety? Rather obviously these questions must, in the last analysis, be answered by the use of experimental methods.

The present discussion concerns itself mainly with the latter of the questions just asked and proposes to give some quantitative data from the laboratory of experimental physiology; unless specifically stated to the contrary all statements are applicable only to an essentially isotonic solution of sodium chloride in distilled water (a 1 per cent solution).

Since as long ago as 1888 the information has been available that at least in dogs and rabbits an isotonic solution (0.7 per cent solution in this case) of sodium chloride in distilled water can be injected intravenously at a rate as rapid as 3.5 cc. per minute and in amounts as great as three quarters of the total body weight of the animal without causing death or, indeed, without precluding complete recovery and an indefinitely prolonged normal life thereafter (Dastre and Loye).

More recent reports emphasizing such matters as "water intoxication" (Rowntree; Helwig, Schutz and Curry), the danger of "speed shock" when solutions are introduced rapidly, even in small amounts (Hirshfeld, Hyman and Wanger), and the possibility of producing wide-spread and presumably dangerous edema when sodium chloride solutions are used (Coller, Dick and Maddock), have tended to foster a critical attitude. It has seemed to us that the time is now ripe for some fundamental studies in which elementary hypotheses should be tested, of which the following study is a sample.

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* Read at the Annual Scientific Assembly of the Society, May 6 1937.

METHOD OF STUDY

Using cats, in which the weights of the various tissues and organs bear approximately the same relationship to the total weight of the body as in the human being and in which the percentage water content of the various tissues and organs is also very comparable, we have determined: (1) The maximum tolerated speed of injection and maximal total dose of 1 per cent solutions of sodium chloride in distilled water, (2) the gross tissue changes which result from just sublethal infusions, (3) the distribution of sodium chloride and water among the more important tissues and organs at the end of the infusion, and (4) the differential elimination of the salt and water by the kidney.

MAXIMAL DOSE AND RATE OF INFUSION

When two important precautions are taken it is possible to inject, without causing death, amounts of 1 per cent salt solution as great as 500 cc. per kilogram of body weight (or amounts of 2 per cent solution as great as 275 cc. per kilogram of body weight) as rapidly as 5 cc. per kilogram of body weight per minute. Infusions less than such maximal amounts are not incompatible with complete clinical recovery within a period of 24 hours or slightly longer, and thereafter animals apparently live indefinitely and normally.

Such doses and rates of injection are, of course, extremely far in excess of those commonly advocated for use in human beings. Hendon's human dose for intravenous injection—an optimum of 200 cc. per hour, or between 4 and 5 liters in 24 hours—is approximately only 10 per cent of the lethal dose computed on the basis of weight by comparison with the cat.

The two precautions which must be taken when using massive infusions are: (a) Relative freedom from "pyrogenic substances" in the distilled water used in preparing solutions, and (b) prevention of regurgitation of gastric contents, aspiration of the regurgitated material into the trachea and bronchi, and drowning of the animal in its own vomitus. The second precaution is by far the more important, inasmuch as the accidental drowning just described occurs in one half or two thirds of nontracheotomized animals long before maximal tolerated doses are even approached (the rabbit is an exceptional animal not requiring tracheotomy because it has a poorly developed vomiting mechanism).

It is probable that increased secretory activity of the tracheal, bronchial, buccal, salivary and intestinal glands act as predisposing causes but it is aspiration-vomiting which precipitates death. When the process is occult no vomitus appearing at the nose or mouth, the real cause of death is not apparent; the increased respiratory movements which initiate the act of regurgitation, the depression in the blood pressure which immediately precedes vomiting, the anticoagulant effect of previously administered solutions on the blood, and the drowning phenomenon itself unquestionably constitute what has previously been called "speed shock." If frothy exudate appears at the nose and mouth just before death from aspiration-drowning, as it sometimes does, the fatality may with equal falsity be attributed to pulmonary edema, and with more reason, since all animals receiving large infusions show variable amounts of pulmonary edema at autopsy. That neither "speed shock" nor fatal pulmonary edema are ever seen in tracheotomized animals in which aspiration-vomiting is mechanically prevented sufficiently, we believe, justifies our conclusions. We believe that, clinically, recognition should be taken of the threat to life which vomiting, stimulated by intravenous infusion, may be, particularly in the case of partly anesthetized or very sick patients in whom the swallowing reflex is either abolished or markedly obtunded. In such patients we would suggest the advisability of continuous gastric drainage during protracted infusions, particularly if moderately fast rates of administration are adopted.

Gross Tissue Changes

The gross tissue changes seen at autopsy after the just sublethal infusions of salt solution which we have used in most of our work involve two types of tissue predominantly, the glandular tissues (stomach, colon, pancreas, salivary glands) and the loose areolar connective tissues. The connective tissues, particularly of the retroperitoneal space and the space between the leaves of the mesentery, show a spectacular characteristic diffuse gelatinous edema; the appearance is similar to that which would result from wide infiltration of these tissues using a hypodermic syringe and needle; unlike such mechanically infiltrated tissue, however, they do not leak solution unless they are strongly milked or "minced" with a knife. The gelatinous edema of the pancreas, which is anatomically placed in the midst of this area, is particularly striking. The edema of the glands of the respiratory and digestive tracts is probably of a different type; it seems to be associated with, and is probably productive of, increased secretory activity, whereas the edema of the connective tissues seems to represent mechanical storage. At all events, during the latter part of large intravenous infusions clear mucoid material drips from the nose and corners of the mouth, secretions accumulate in the stomach and intestine, and diarrheic feces are discharged in profusion from the anus indicating hypersecretion of the glandular structures of the digestive tract.

The peritoneal cavity contains considerable fluid, but the pericardial and pleural cavities contain relatively little. The lungs are invariably edematous, but the extent of this edema is very variable from animal to animal. Cerebral edema is never seen.

Distribution of Salt and Water Among the Tissues and Organs

The skin and the muscles, which together constitute nearly two thirds of the entire bulk of the body and considerably more than two thirds of all the soft tissues of the body, increase both with respect to salt content and also with respect to water content as a result of infusion. Chemical analyses show that this increase in salt and water is of almost precisely the order which should occur on the supposition that these tissues passively store the infused solution in the concentration in which it is originally presented to them, viz., as a 1 per cent solution. Notwithstanding the comparatively great bulk of these tissues, the actual percentage of the total amount of the infusion which they can thus store is quite small, approximately 20 per cent. The other organs of the body, because of their relatively small bulk, are of no practical importance as reservoirs for infused solutions. In connection with a statement previously made that the edema of the glandular organs is probably intimately associated with secretory function, it is of interest to note that the glandular organs very definitely do not follow the rule for the muscles and skin; they store much more water than salt and are apparently engaged in differential secretion of water.

The cerebrum exhibits a peculiarity which it shares with no other tissue; although it actually loses in water content as a result of infusion it gains considerably in salt content. The fact that it does not gain in water content definitely disposes of the theory that the cause of death in massive infusion is cerebral edema; it furthermore means that the cause of death is not "water intoxication," if cerebral edema is actually the cause of death in water intoxication, as some recent experimental investigations would seem to indicate.

The fluid in the peritoneal cavity is actually of considerable significance from the point of view of storage capacity. Its composition is practically that of a 1 per cent salt solution, i.e., the peritoneal cavity secretes, or at least stores, fluid in approximately the same salt concentration as the infused fluid. Approximately 10 per cent of the total bulk of the infusion thus appears as stored fluid in the peritoneal cavity; actually, the amount is probably somewhat in excess of this figure, since we have certainly been unsuccessful in evacuating all the fluid from the various peritoneal crypts and folds.

ELIMINATION BY THE KIDNEY

The excretory activity of the kidney is markedly and rapidly stimulated by intravenous infusion. Thus, because a considerable period of time elapses between the commencement of the infusion and its completion, a certain amount of the infused salt and water never requires storage but is excreted forthwith. During our infusions, which have lasted, on an average, 115 minutes, between 15 and 20 per cent of both the salt and water has been eliminated.

Counting the elimination by the kidney, storage in the abdominal cavity and in the muscles and skin, we can account for only approximately 50 per cent of all the infused salt and water. The discrepancy is tremendous, considering that virtually the only unanalyzed tissues of any bulk are those of the bony skeleton, which certainly can provide little storage for water and presumably as little storage for salt. For the apparent discrepancy there seems to be only one explanation. This is that the connective tissues, which normally have but little bulk, become tremendously distended during infusion. At present we have little actual evidence to substantiate this hypothesis beyond the remarkable and wide-spread edema of the connective tissues visible through the thin peritoneum. Perhaps it is a little difficult to believe that the connective tissues in their most distended condition are capable of storing so much solution, but the distribution of such tissues throughout the body is, of course, wide-spread, and we have carefully analyzed virtually every other tissue.

Urinary excretion continues after the cessation of the infusion at a very rapid rate until, within 24 hours, all of the salt and about four fifths of the added water have been eliminated. This elimination, of course, completely restores the salt balance, but it still leaves a relatively considerable amount of the water in the tissues. We have not yet determined the location of this retained water nor how soon it is eventually eliminated. This finding, however, of water retention after infusions of saline solution is not a new observation; the only novelty is the discovery that it occurs at a time when chloride excretion has far outstripped water elimination, in short, that the water retention is not associated with, or due to, salt retention.

This communication is not intended as a brief for intravenous therapy in general or for larger and more rapid infusions in particular. No implications are made as to the indications for intravenous infusion as such or that in case such therapy seems desirable the vehicle should be salt solution in whatever concentration. Our intention is rather to indicate the tremendous capacity of the normal body for essentially physiological salt solution when injected intravenously, if ever and whenever the method may seem clinically advisable. Perhaps an understanding of this capacity will steady the hand and calm the fears of the overtimid practitioner who may see his patient in dire need of water which he cannot take by mouth and which the practitioner might otherwise fear to give by vein lest he transgress safe limits of dosage or speed of injection. In the meantime, for the overzealous or the overbold, we would hold out the warning that the real menace is neither speed nor bulk but the purely adventitious matter of aspiration-drowning, a menace which is almost sure to rear its head long before any intrinsic danger of overloading the patient or his circulation could arise. It should also be emphasized that no conclusions here drawn are now known to apply to any solution but salt solution and then only to essentially physiological solutions, not to hypertonic solutions.

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RENAL TUBERCULOSIS*

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Until quite recently, renal tuberculosis if demonstrated to be unilateral was considered to be a definite indication for reasonably prompt, though not hurried nephrectomy. This opinion was generally held and was based on extensive pathologic and clinical studies. These had shown that the disease was often unilateral and that it never healed to complete cure of the involved kidney. Experience also showed that, in unilateral infections, nephrectomy resulted in cure in about one half of those operated upon; while, in cases apparently bilateral, if the organ showing the greater involvement were removed, there was often an amelioration of the distressing bladder symptoms that were generally a prominent clinical feature of the disease, and, rarely, a cure might be secured.

The disease has been studied and treated, using every modification and improvement in diagnostic and therapeutic technic that has been made available since the discovery of the tubercle bacillus by Koch in 1882. Prominent among these are the use of the X-ray, cystoscopy and ureteral catheterization, pyelography and the tremendous advances that have been made in the treatment of tuberculosis since 1900. A definite hindrance to the study of the details of renal tuberculosis has been the difficulty in producing, in experimental animals, renal lesions that are at all comparable in their character and course to those observed clinically in man. This is due in part to the inaccessibility of the kidneys and in part to the arrangement of their blood supply, which is such that artificial infection of them, without at the same time drenching the whole vascular system of the animal with bacilli and producing a disseminated miliary tuberculosis, is exceptionally difficult. This would naturally defeat the object of the experiment insofar as producing a chronic caseous lesion in the kidney was concerned. Coupled to this, the slow evolution of the disease, difficulties in culturing the organisms, imponderable variations in the virulence of different types and strains of bacilli and in the immunity factors of different experimental animals, have served to hamper the successful solution of many difficult problems.

Despite this, renal tuberculosis became recognized as a disease of hematogenous origin, with a very uncertain evolution, presenting unaccountable relapses and remissions, both clinical and in the number of bacilli excreted in the urine and of indefinite duration. It was thought to be always exemplified quite early, usually by evidences of a painful cystitis but sometimes by hematuria or some other genito-urinary symptom, and occasionally it was disclosed at an operation undertaken for some other renal condition.

The urinary findings were thought to be fairly constant: a distinct albuminuria plus a more or less marked pyuria, without the presence of ordinary bacteria on simple stain, but with tubercle bacilli demonstrable, in some way or other, in practically every instance. The albuminuria was so constant a finding that, if it were absent in the presence of an otherwise unexplained pyuria, tuberculosis was considered to be extremely improbable and search for the bacillus, more often than not, was omitted.

The disease, if once established, was considered to be progressive and ultimately fatal, either from involvement of both kidneys or from one or other of the numerous complications that may develop and cause death in any tuberculous individual.

More recently, experimental (Medlar and Sasano), postmortem (Medlar), and clinical (Harris; Thomas; Thomas and Kinsella; Woodruff and Bumpus) evidence has been brought forth which indicates that many of the conceptions of renal tuberculosis, as they were known, may have been in error despite the mass of clinical experience that had gone to support them.

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* Read before the Society, April 21, 1937.

Summarized, these views are that the presence of tubercle bacilli in the urine from a kidney always means tuberculosis of that organ (Lieberthal and von Huth); that the incidence of renal infection in the presence of tuberculosis of other organs is higher than has been suspected, is frequently bilateral and is marked by an invasive stage during which symptoms are almost nil and urinary signs are not characteristic at all; that the renal lesions of tuberculosis tend to heal as do similar lesions in other organs and that they may be divided clinically into nondestructive and destructive types, surgery being permissible in the latter but not in the former. The result of all this is that some surgeons have hesitated to remove a kidney for tuberculosis lest they either sacrifice an organ that might be saved or lest they fail to secure a cure because of an asymptomatic preclinical lesion in the opposite kidney. Certain phthisiologists have construed the word "healing" as used in the studies cited, to mean "cure," with the result that patients with well-demonstrated unilateral caseous renal tuberculosis are sometimes denied the relief and prospect of cure that a prompt nephrectomy might give them.

It is not difficult to reconcile the increased incidence both as to occurrence of renal lesions and their bilaterality in the experimental work and the postmortem studies published; each of the kidneys studied was from a heavily infected animal or from a human being who had died from the disease and in all of which considerable dissemination of the bacilli might have been expected. The same is true of the studies of sanitarium cases reported. The existence of an asymptomatic preclinical stage may readily be explained on the basis of the incubation period that is characteristic of every infection; since little or nothing is known of its duration in human tuberculosis of other organs, it is not surprising that it was noted for the renal lesion once the matter was investigated carefully. Likewise, the commonly observed uncertain course, sometimes with long periods of latency, may account for the clinical remissions noted under nonsurgical treatment and for the evidences of healing observed. That healing occurs in renal tuberculosis, largely evidenced by fibrosis, has long been noted; every tuberculous kidney, no matter how much disorganized by the disease, shows it in some degree, but I have not been able to find a report in the literature of any kidney in which it has become quite satisfactory with a complete disappearance of the caseous areas, bacilli, giant cells and round cells, leaving only a scarred kidney secreting a normal urine.

Not finding any reason for delaying surgery, from the articles located in a fairly diligent search of the literature, I turned to the records of my own patients in whom renal tuberculosis had been diagnosed and treated by myself or others, with a view of learning from them whether a change should be made in my practice. I have made an earnest effort to get in touch with each patient and, if possible to examine each one myself.

It is impossible to adjust the statistics of such a small number of cases as I have encountered so as to give a fair summary as to details or the course of the disease, but, if the cases are arranged in 2 groups depending on whether nephrectomy was done or not and the final index made on the end-result, an approximation of accuracy may be won. This approximation is enhanced, if, in considering nephrectomized cases in renal tuberculosis, no cure is accepted unless the patient has been followed for at least a year after operation and cessation of symptoms or signs can be shown to have been extended well beyond that time; while any continued evidence of bladder irritability or any persistent abnormality of the urine whenever shown is considered as evidence of possible remaining or recurrent tuberculous infection, even though the patient may have been quite well with a clear normal urine for a certain period during the interval. These requirements may offset, to a certain degree, the fact that, following convention, nephrectomy was recommended in every instance in which it did not seem to be contraindicated and was performed whenever permission was obtained.

In the 27 cases of which I have adequate record (about 1 to 220 of urologic patients seen in 17 years), nephrectomy was done in 19 instances (70 per cent), 12 by me and 7 by others. Of these there was 1 operative death (5.3 per cent) (No. 7, personal). Two others (10.6 per cent) (Nos. 4 and 15, operated upon elsewhere) are known to have died, probably from tuberculosis, 1 a short time, another 5 years after operation, although neither could be traced with certainty. This makes a total death rate for operated cases of 16 per cent. Of the remainder, 8 (42 per cent) (6 personal, 2 elsewhere) are known to have been living and apparently well from 2 to 13 years after nephrectomy. All are free from bladder symptoms, and of the 8, 5 (26 per cent) (Nos. 8, 10, 16, 17, and 22) have had urinalyses done, so that there is little doubt as to their cure for the time limits set down. Seven (37 per cent) of the others (4 personal, 3 elsewhere) have been set down as improved. One (No. 11) had a partial remission of bladder symptoms for 10 years after operation, although his urine did not clear and he was shown to have had tuberculosis of his lone kidney 3 years after operation; a second, (No. 18) had nocturia of 3 and red blood cells in her urine 6 years after operation; a third (No. 23) had albumin and pus 3 months after operation, but her physician says that, when last seen, 2 years after operation, she was quite normal. A fourth and fifth (Nos.21 and 27) have been observed for less than 1 year after operation, while a sixth and seventh (Nos. 5 and 24) have developed tuberculosis in a lone kidney 2 and 16 years after operation. One case (5 per cent) (No. 25) remains unimproved 8 months after a difficult subcapsular nephrectomy for closed tuberculosis; she had had 3 relapses and 3 apparent cures since the disease had first been diagnosed 5 years before.

These statistics are not impressive as an argument for operative cure of the disease, but if they are contrasted with cases in which no operation was done the advantage of surgical over an exclusively medical treatment becomes evident. Of the 8 (30 per cent) not submitted to nephrectomy, 2 (25 per cent) (Nos. 2 and 19) are known to have died from tuberculosis, 1 (No. 2) in the hospital and 1 (No. 19) in a sanitarium shortly after having left the hospital. Three others (36 per cent) (Nos. 3, 9, and 12), were not located but may reasonably be presumed to have died either because of the extent of their lesions (multiple tuberculous foci) or of age (55 and 69 years) when last seen 18 and 12 years ago, and are considered unimproved. Considering known ability to support life and carry out ordinary duties as improvement, 2 patients (25 per cent) (Nos. 20 and 26), commented on below, are living but with tuberculosis 5 years and 8 months, respectively, after the diagnosis was made; and one (13 per cent)(No. 6) is cured of his bladder symptoms, although he still has albuminuria and a functionless right kidney, probably "closed" tuberculosis 16 years after the diagnosis was first made. Of definite known cures in this group, there are none.

The most interesting group for study in connection with the question whether to operate or not is that of those not operated on but who nevertheless show improvement. A conspicuous example is a man, aged 38 years (No. 6), who had had right renal pain and hematuria for 6 months before coming under observation. Study showed right renal tuberculosis and poor function of the left kidney, the reason for which was not established, so that nephrectomy was refused lest an anuria or uremic death ensue. He was placed on tuberculin treatment. Fourteen months later he developed right epididymal tuberculosis. Now, at the age of 55 years, 16 years after the disease was diagnosed, he is apparently well and works each day. His right testicle is atrophic and both epididymes slightly nodular. He has no frequency or pain on urination, and his urine is clear but contains a few hyaline casts and red blood cells and a large amount of albumin. On the X-ray film several opacities suggestive of caseous areas are present in the shadow cast by the right kidney; the shadow cast by the left kidney is larger than that cast by the right and is apparently clear. On the intravenous urogram a functionless right kidney is shown, and the left one is probably normal although the minor calices do not show up well.

A second case (No. 20), occurring in a woman aged 32 years, had suggestive symptoms dating back 4 years. On examination both kidneys were shown to be about equally involved, so that it was felt that nephrectomy was contraindicated. She spent a short time in a sanitarium without marked improvement, but she has had a child since and is living today, still having renal tuberculosis confirmed recently by another urologist, 5 years after the diagnosis was first made.

The third improved case (No. 26) occurred in a man, aged 42 years, who had had epididymal tuberculosis at the age of 14 and various pulmonary incidents during the interval. Eight months before reporting last he had had an attack of painful frequent urination of short duration and had been refused life insurance on the basis of albumin and pus in the urine. Examination showed right renal tuberculosis with a partially calcified cortical abscess. He refused nephrectomy and went on a fairly rigid rest cure. Several urinalyses during the past 8 months have shown pus and cocci but no albumin or tubercle bacilli. Undoubtedly a part of the focus in the right kidney has walled off and the excretion of tubercle bacilli has lessened if not ceased altogether. It is probable that this focus will either break forth again as an open lesion or result in a closed pyonephritis, making a very much more difficult operative problem than is present now, unless some other accident or illness carries him off.

No definite conclusions may be drawn from this study except that the cases subjected to nephrectomy have done better than those not operated on. This, of course, may be because those operated upon have had a better resistance to tuberculosis than those who have had only medical treatment. Other imponderable and incomputable factors may have entered into the end-result, but the number of cures in the nephrectomized cases and the total absence on any completely demonstrated cure in those not operated on indicate that nephrectomy gives the patient a certain advantage that he does not have without it. Accordingly, I do not expect to change the practice of operating when the disease may be shown with reasonable certainty to be unilateral in a patient who is otherwise capable of withstanding operation and who has no very active or extensive extraurogenital tuberculosis. Certain impressions have grown from the study I have made of the literature and in following these cases, which I wish to put before you:

1. Active caseous renal tuberculosis may be present without either albumin or pus in the urine (No. 15). However, this is very unusual, and, if repeated examinations are made of the urine of a patient who has renal tuberculosis, one or other or both of these urinary abnormalities will show up eventually.

2. Albuminuria, in the absence of pus, in an individual with evident extraurogenital foci of tuberculosis or a history of them, may mean renal tuberculosis either "open" or "closed" (Nos. 6, 16 and 25). Practical considerations, largely those of expediency, will determine whether the case should be worked up thoroughly and submitted to nephrectomy or not. I believe that all should, because, since closed renal tuberculosis will not heal completely, constant absorption from the purulent and caseous renal mass may cause secondary effects in remote organs (myocarditis, nephritis, etc.) which will prejudice health or life, apart from the hazard that arises from the tuberculous nature of the focus itself (dissemination, extension, meningitis, etc.). One must decide whether the hazard from this is greater than that from nephrectomy.

3. Even a short period of complete rest (2 months) (No. 27) for a patient in whom technical difficulties are so great that a sufficiently accurate diagnosis to warrant nephrectomy cannot be made may so improve him that a definite conclusion may be reached and nephrectomy carried out successfully.

4. The best results are obtained by coöperation between the urologist and internist both before and after nephrectomy. Under the best circumstances, renal tuberculosis is a very serious disease, and unless due care is taken to determine the presence and character of remote tuberculous foci all that might be expected from nephrectomy will not be gained. The operation is but one part of the treatment, and observation must be carried out for years.

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SUBCORTICAL PREFRONTAL LOBOTOMY IN THE TREATMENT OF CERTAIN PSYCHOSES*

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The operation of prefrontal lobotomy was devised by Egas Moniz somewhat over a year ago for the relief of certain mental symptoms that proved rebellious to conservative treatment. The experimental data and clinical experiences leading up to this new surgical treatment need be stressed only briefly, since the so-called frontal lobe syndrome is fairly well established. Foremost among the experimental data should be considered the findings of Fulton and Jacobsen who were unable to produce behavior of a type characterized as neurotic in animals whose prefrontal areas had been extirpated. Among the clinical observations the careful studies of Brickner and of Ackerly on men whose prefrontal areas had been more or less completely removed for the extirpation of tumors are most important. In these individuals there was notable lack of preoccupation with self, a disinclination to worry, which, in Ackerly's case was of annoyance only to the patient's husband, since the woman would not sit down with him and discuss the parlous circumstances of the family.

Moniz attempted, by partial destruction of the subcortical white matter of the prefrontal areas, to reduce the symptoms of pathological worry, anxiety, apprehension, nervous tension and other manifestations of some of the psychoses in which no anatomic deviation could be found to account for the syndrome. He argued that in these cases there was abnormal stabilization of the synaptic patterns, and that forcible interruption of these would result in a return to a more variable and fluid type of reorganization. He has now extended his series to about 50 cases, and in a recent article reports some apparent recoveries in schizophrenics. His results have been best, however, in the agitated depressions, the involutional psychoses and in the severe anxiety neuroses. Our first results seem to confirm his findings.

OPERATION

The technic of operation is relatively simple. Two burr holes are placed 3 cm. to either side of the midline and 3 cm. in front of the interaural line. After opening the dura and securing hemostasis, a special cannula with a cutting loop is inserted through the cortex in such a direction that it will penetrate to the white matter beneath the lateral aspect of the cortex of the prefrontal area, and by means of the loop 3 cores about 1 cm. in diameter are cut at depths of 4.5, 3.5, and 2.5 cm. The leucotome is then withdrawn and re-inserted so as to cut the white matter beneath the mesial cortex at depths of 4, 3 and 2 cm. The operation is then performed on the opposite frontal lobe, making in all 6 cores in each prefrontal lobe, and interrupting, at an estimate, from 15 to 25 per cent of the axis cylinders in each lobe. There is seldom any significant bleeding. We have recently gone deeper into the frontal lobe and have also introduced a detail that reveals the location of the cores, namely, the injection down the needle track of a small quantity of Thorotrast; and we have devised a special leucotome (made by Lentz) that facilitates this. The wounds are closed with silk sutures that can usually be removed on the fourth day.

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Local anesthesia is the method of choice, but in apprehensive patients, avertin followed by gas or ether has been used. There is no significant alteration in pulse or respiration during the operation, and the patients have suffered no shock. They have been returned to bed in the semi-sitting position, take solid food the next day, are out of bed usually on the fourth day, and sometimes can go home in a week. In our 20 cases followed more than 6 months there has been some vesical disturbance in 6, no pupillary disturbances, and only 1 case of pronounced reflex changes, presumably dependent upon postoperative thrombosis of a wider area. This patient made a complete recovery in a few days, the Babinski sign and reflex grasping disappearing rapidly and the perseveration of speech after a few days.

General Effects

Alterations following operation have been especially notable in the peripheral circulation. The cold moist cyanotic hands tend to become warm and pink immediately following operation and to remain so for a considerable period. They do not present the dryness characteristic of sympathectomized limbs, and if the patient becomes emotionally upset a return of the coldness and pallor may be observed. In 1 case the change in circulation was so pronounced that about 2 weeks after operation there was desquamation of both palms. In another case, in which the operation was done in 2 stages, the homolateral hand became warmer and drier after each operation, and a day after the second operation both hands were warm and pink and have remained so. Similar changes occur in the lower limbs. As one patient expressed it: "I used to pile up the covers 'til I'd nearly suffocate, but I couldn't get my feet warm. Now they're warm all the time."

In a fourth patient there was a history of rheumatic heart disease with auricular fibrillation that proved resistant to digitalis in emetic doses. Three days after operation the rhythm was regular, and for the first time a presystolic murmur was audible. Some 10 days after operation, when the patient was at home, she became emotionally upset at the jests of her friends, and the fibrillation recurred. Congestive cardiac failure set in, and the patient succumbed 4 months later.

Alterations in blood pressure have been noted repeatedly. Indeed, in 1 patient the oscillations were sufficiently severe to indicate a localized cerebral effect, since for days there were hourly variations of as much as 30 points. With recovery, the blood pressure became stabilized at about 130 mm. Hg. systolic. A reduction in the systolic blood pressure from 170 during the agitated phase to 140 in the aftermath was observed in another case.

The functioning of the gastro-intestinal tract can only be inferred from the statements of the patients. Several have been observed who complained bitterly previous to operation of indigestion, gas, bloating, constipation, hemorrhoids and the like, but who in the postoperative period have remained comfortable. One of them in particular, whose preoccupation with elimination was obsessive, received complete relief for a period of 6 weeks, but is now undergoing a gradual magnification of the complaints.

Psychologic Effects

Abstract thinking, constructive imagination and synthetic ability seem to be impaired to a greater degree than more fundamental intellectual processes. Our patients can name colors rapidly, add columns of figures correctly, remember recent and remote events exceptionally well, concentrate upon their tasks with less distraction than before, pick correctly the cups that hide the pennies after 90 seconds, read and write rapidly. The response to the donkey story and to the cowboy story has shown rather marked defects in synthesis. Patients can often remember the details of the stories quite well, but when it comes to drawing the moral, they are stumped. They can manipulate dominoes quite well, but when it comes to building a fitted square, 7 on a side, they easily become blocked and take some time to extricate themselves. In building a 3-inch cube out of 27 1-inch cubes, so that the outside shall be painted, they take an undue time and occasionally build extraordinary figures not even resembling cubes. Even with help and suggestion, this is difficult for them. In the "stepping-stone" maze many patients are unable to find the correct pattern after 6 or more trials, make just as many mistakes on the last as on the second trial, and become fatigued. In the word-association tests, definitions and synonyms are given, even though it is specifically stated that such answers are not necessarily desired. Improvement in performance has been noted as time goes on.

SYMPTOMS RELIEVED

Agitation is reduced in all of the patients. One man, under local anesthesia, and as the scalp was being sutured, stated that he felt the vague uneasiness that had dominated his life for years melt away, and in spite of persistence of his neurotic behavior has maintained vigorously this attitude. Our first patient, whose psychosis had progressed to the point where she postured nude in front of the mirror and where she could hardly remain in bed for examination, was utterly calm upon coming out of the anesthetic. Patients in panic and in catatonic states have returned to a state of much greater accessibility. In 1 patient, a catatonic of 3 months' duration, the operation was performed in 2 stages a week apart. There was no substantial relief of the catatonic picture following the operation upon the right side, although temporary accessibility was gained through the injection of sodium amytal intravenously. At the end of 5 days the patient was rigid, incontinent and tube-fed. The second operation was performed without even draping the patient, the burr hole having been made previously. As the leucotome was making the cores, the patient's pupils contracted, her facial expression became startled and she reached up with both hands. For 2 days thereafter she remained catatonic, not even responding to sodium amytal or to carbon dioxide. Thereafter she improved progressively, accepting food the third day, eating it herself the next, washing herself the following, walking the day after, talking on the tenth day, using the telephone on the fourteenth; and she has now resumed her life in the family circle and believes that she could soon get back her job.

Obsessions and compulsive behavior have shown immediate improvement, although in some cases there have been relapses. One patient, who for 35 years had been obsessed with ideas of contamination and whose life was a burden on account of them, lost them for a period of 6 weeks, after which they gradually recurred following some encounters with a pet dog, dogs being her special abomination. This patient was subjected to a second and more extensive operation in March and is now at home in better condition. Another young woman with a 12-year fear of syphilis is back at work as a telephone operator and is doing well. The loss of the obsessive nature of the ideas is particularly interesting. As 1 man, with a simple depression of 10 years' duration said: "You haven't done anything to me. I'm just as bad as I ever was. My business is ruined, my family's gone to pot, I'll never be any good again." He was asked: "Well, are you worried about it?" "No," he said, "Say, Doc, what have you done to me anyway?" It appeared upon questioning that he was able to evoke the memories of his former attitude and also had perfect realization of the serious state of his business, but the obsessive quality of these ideas was no longer present. He was able to smile for the first time in 5 years. The improvement was being maintained at the latest report 2 months ago.

Another patient who had spent 2 years in bed on account of a supposed arthritis and who flinched and screamed whenever her back was touched, a patient whose previous history showed her to be a confirmed neuropath, walked on the third day after operation, sprained her ankle on the fourth but continued walking, and is now taking care of her household in a rather satisfactory manner. The breaking through of an established pattern of behavior seems to be one of the features of many of our cases, and the lack of constructive imagination, of abstract thinking, seems to be a positive benefit to these patients. To coin a word, these patients have been relieved of anterograde algimnesia, the painful remembrance of things that will never happen.

The improvement noted immediately after operation has not been maintained in about a third of our cases. The old phobias return progressively in some cases, and the episodes of excitement, particularly in the schizophrenics, make working adaptation impossible at present. Whether improvement will occur in these cases later on is questionable. Five out of 6 schizophrenic patients are unimproved, although not confined to institutions. The catatonic girl in whom a 2-stage operation was performed, and incidentally a more extensive operation, seems to be doing well; but catatonics are likely to do better than other patients with schizophrenia. Three out of 5 patients with agitated depression are maintaining their improvement. One died postoperatively of cerebral hemorrhage, probably incidental rather than caused by cutting an artery, and 1 is in an institution because of a preoperative suicidal attempt by gas that almost succeeded. Following the operation the depression cleared up to a great degree, but the confusion and forgetfulness and restlessness made it impossible to care for her at home. She is slowly improving.

Relapses will probably increase as time goes on. We have noted, however, that those patients whose postoperative condition was the most favorable have been the ones that tended to relapse. Where a rather long period of confusion, disorientation, inertia, semistupor, forgetfulness and the like has been present, the ultimate results have been better. Apparently one must disturb these patients seriously in order to obtain satisfactory remissions. This was attempted in a recent case by making the cores farther back, but the motor zones were encountered, and this schizophrenic girl now has a brachial monoplegia, and the disturbing ideas have recurred. More wide-spread transection of the axis cylinders farther forward seems to be more effective and less disabling.

Of the 20 cases operated on last year, 7 are substantially well from 7 to 10 months, and 5 are improved, 6 unimproved and 2 dead. Two are in an institution, and 2 institutional patients are at home. Three patients have resumed their jobs.

In the choice of cases, the social aspects have been of greater significance to us than the diagnostic categories. We have operated on patients whose outlook for recovery was rather poor or who were faced with disability or suicide, and whose occupations did not require a great amount of creative imagination. Though far from satisfied with the results, we are encouraged to proceed, since the ability of these patients to adjust has not been materially impaired, and many of them are definitely more comfortable. Psychologic tests, as far as we have carried them, reveal no serious disability, and thus far there has been no instance of psychopathic behavior, with the exception of 1 patient that became intoxicated as he was accustomed to do before operation.

THEORETICAL CONSIDERATIONS

The question of the manner of action of prefrontal lobotomy is an interesting one, and far from solution as yet. The theory of breaking up pathologically stabilized synaptic patterns as expressed by Moniz, is possibly a little naïve. The interruption of the pathways between the prefrontal areas and the hypothalamus, if such pathways exist, might divorce the ideational elements from their emotional components, might "de-afferent" the emotional "gland" of the hypothalamus, as it were. We have noted some loss of initiative, of spontaneity; our patients admit being a little subdued. If there is a driving force to the personality, and if this is located in the prefrontal areas, a suggestion that is also unproved, some of the effects might be due to a lowering of the psychological tension. Ackerly's patient expressed her condition quaintly but graphically when she said: "Doctor, you've cut out my worry center." Another way of expressing the phenomenon might be that the blocking observed in many of the patients is relieved by cutting down upon the number of pathways by means of which ideas crowd in upon one another. A host of other explanations might be advanced with equal justification, such as whittling down the super-ego, and simply resting the brain by reducing the pathologic overactivity through elimination of so many millions of ganglion cells. But the possibility that the operation is just another "shock" measure does not deserve serious consideration. The operation is not a shocking one, and the good results may be delayed for a time.

CONCLUSIONS

Subcortical prefrontal lobotomy has been performed in 25 cases with 1 death from cerebral hemorrhage and 1 brachial monoplegia. Seven patients are substantially well, and 5 are improved. Affective disorders seem to offer much better prospects than schizophrenic. The reduction in the obsessive nature of the painful ideas is the outstanding result. Signs of intellectual deficit are not very pronounced and do not handicap the patients for ordinary occupations of a routine nature, even in the business world. No new psychopathic symptoms have developed. Patients with pronounced initial deficit seem to make more substantial recoveries than do those who are in excellent condition immediately after operation. Theoretical considerations of the modus operandi are given without insistence.

ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"SURGERY OF THE SYMPATHETIC NERVOUS SYSTEM IN RELATION TO CARDIOVASCULAR DISEASE,"* **James C. White, M.D.**, Boston.

Advances in surgery of the nerves to the blood vessels and heart began largely as a result of trial and error, but during the past decade this new form of neurosurgery has achieved a firmer foundation based on anatomical and physiological principles. The purpose of this paper is to trace the development of present-day procedures in this field. Raynaud's disease and allied vasospastic disorders can be improved by cutting the vasoconstrictor nerves, but in the past these operations have often been disappointing. Novocaine block of the sympathetic ganglia and other accurate diagnostic tests have eliminated 1 frequent cause of failure by facilitating the selection of suitable cases uncomplicated by occlusive arterial disease. After careful selection of patients with excessive vasoconstrictor activity in the legs, lumbar ganglionectomy is a uniformly successful operation. A reason for the inferior results after cervicothoracic ganglionectomy for Raynaud's disease in the arms has recently been discovered. This lies in the action of circulating hormones, adrenalin and sympathin, on smooth muscle after degeneration of its nerve supply. For reasons which were illustrated by animal and human experiments, this phenomenon is slight after lumbar ganglionectomy but may cause striking residual vasospasm and color changes in the hands after cervicothoracic ganglionectomy. A new and more physiological operation has been developed to avoid this complication, and the results of this procedure are highly satisfactory. The early surgery of angina pectoris, which began in 1916 with the cervical sympathectomies of Jonnesco, was only partially effective because of inadequate anatomical knowledge of the cardiac nerves. The recent discovery of the accessory thoracic cardiac nerves has demonstrated the need for destruction of the upper thoracic sympathetic connexions if the viscerosensory paths to the heart are to be completely interrupted. When the upper 5 thoracic sympathetic ganglia, their cardiac rami, or the corresponding posterior spinal roots are destroyed, cardiac pain is abolished. This has been found to apply also to intractable pain from aortic aneurism. Furthermore, there is early evidence that certain tachycardias can be controlled by interrupting the cardiac accelerator nerves which run in the same trunks. These findings are based on animal experiments and on observations of over 60 operations on human sufferers from intractable cardioaortic pain.

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PARALDEHYDE-BENZYL ALCOHOL OBSTETRICAL ANALGESIA BY THE KANE-ROTH METHOD*

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The relief of pain during labor and delivery has been the objective of obstetricians for many years, but practical success has only been attained in more recent times. Many hypnotics and anesthetics have been tried and recommended for the production of analgesia and amnesia in labor. The present feeling is that a parturient woman should be given whatever degree of analgesia and anesthesia it is possible for her to have with safety to herself and her child. When the woman is spared this pain and suffering, the psychic and physical strains are abolished and a more rapid and satisfactory postpartum recovery is effected.

During the past few years there have been many reports in the literature on the use of paraldehyde to secure relief of pain during childbirth, the method of administration being per rectum (Rosenfield and Davidoff; Colvin and Bartholomew; Kane and Roth; Moore and McCurdy; Conn and Vant). More recently, it has been tried orally (Douglass and Peyton). At the present time the reports, which are increasing in number, have established it as one of the more successful methods.

The method which I wish to present is the one perfected by Drs. Howard F. Kane and George B. Roth, of the George Washington University School of Medicine. It was my privilege to have been associated with Dr. Kane during the inception and perfection of this method of relieving pain during labor. This technic has been used extensively by many obstetricians of this city, and on the ward services of the George Washington University, Garfield Memorial, and Gallinger Municipal Hospitals. A recent series has been reported from Cleveland by Moore and McCurdy, of the Western Research University, in which, after various technics were employed, the method and dosage used in the Kane-Roth technic produced the most satisfactory results. In their series of 100 cases, they report adequate analgesia and amnesia in 76 per cent, whereas in 4 per cent the method failed entirely.

The pharmacology of paraldehyde and benzyl alcohol has been adequately described by Kane and Roth. Their observations, together with those of Douglass and Peyton, and of Knoefel show that paraldehyde is a safe and promptly acting hypnotic, having a wide margin of safety between the toxic and therapeutic doses. Benzyl alcohol also is of low toxicity; furthermore, the small amount used in the mixture can be considered negligible as regards its general narcotic effect. Its purpose is to anesthetize the rectal mucosa until the paraldehyde is absorbed. Emphasis should be placed on the purity of the two drugs.

Clinically, this method has been used in patients with heart, kidney and liver disease as well as in normal cases, with no apparent harmful effects. To obtain satisfactory analgesia and amnesia, the mixture should be administered as soon as the patient complains of pain. When under the effect of the paraldehyde-benzyl alcohol mixture, the patient usually sleeps quietly, occasionally stirring slightly with each contraction. Moore and McCurdy, using the Dodek hysterograph to study the effect of paraldehyde upon the uterine contractions, concluded that there results a momentary period of relative uterine inertia, but within 15 to 20 minutes the contractions regained their previous character. They further concluded that paraldehyde does not materially slow labor. This agrees with the observations of others, and with personal observation.

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* Read at the Annual Scientific Assembly of the Society, May 5, 1937.

Excitement and undue restlessness of the patient usually indicate that the dosage has been inadequate, that the effect is wearing off, that the presenting part is soon to be born, or more frequently, that there is poor absorption of the drug from the rectal mucosa, due to the presence of fecal material.

The ultimate success obtained has been shown to depend upon the length of labor and the parity of the patient. It is much better in primiparous patients, in those patients in whom the medication was begun early in labor, and in all types of cases in which labor was of more than 4 hours' duration. Spontaneous delivery may be accomplished by this method, but delivery by forceps under a general anesthetic, preferably ethylene-oxygen, has been the method of choice.

As it is my custom to immediately resuscitate by the Kreiselman Apparatus all babies who do not breathe and cry spontaneously following delivery, I have not observed any increase of fetal asphyxia or apnea. In a complete review of all the present literature on the use of paraldehyde during labor, I have not found any maternal or fetal death reported that could be attributed to the drugs.

Technic of Administration

At the early onset of labor, the lower bowel and rectum should be thoroughly emptied by an initial soap-suds enema, followed by irrigations of normal saline solution until the return is clear.

As soon as the patient begins to complain of pain, the paraldehyde-benzyl alcohol mixture is administered. The dose of paraldehyde is 1.2 cc. to each 10 pounds of body weight. The dose of benzyl alcohol remains constant at 1.5 cc. To the estimated amount of paraldehyde is added the 1.5 cc. of benzyl alcohol, and this mixture is instilled into the rectum by gravity, by means of a funnel and a large catheter, which has been lubricated and inserted about 10 cm. (4 inches). This is followed by not more than 30 cc. of normal saline solution in order to wash out the catheter and distribute the mixture. The catheter is then withdrawn and the buttocks firmly compressed for a short time to insure retention of the mixture.

If the patient is not asleep one half hour after the initial instillation of the rectal solution, one fourth grain of morphine sulphate is given subcutaneously. Although it is rarely necessary to repeat the morphine, occasionally in long labors it has been repeated with no apparent harm.

Following the above technic, further medication is based entirely upon the patient's reaction and the degree of analgesia and amnesia obtained. The prescribed dose and always the full dose may be repeated, if necessary, $1\frac{1}{2}$ hours after the first. As the progress of labor continues, it will be found that the effect of each successive injection is more lasting, and the interval between doses extends to 3 to 6 hours. After 2 or 3 rectal injections have been given, the rectum should be irrigated with warm normal saline solution to insure absorption of the succeeding injection.

To prevent dehydration of the patient, a glass of orange juice or water is given before each rectal injection. The patient usually can be aroused sufficiently to drink the fluid; if not, dextrose solutions may be given intravenously, particularly in prolonged labors.

As the patient is not conscious of distention of the bladder, she should be catheterized every 8 hours, or oftener if necessary.

As the ultimate aim of the technic is to insure obstetric analgesia and amnesia, emphasis is to be placed on the necessity of repeating the rectal injection when the patient begins to arouse and awaken, and not to wait until she has become restless.

The above method, when administered properly, should give uniformly good results in the great majority of cases. There is one variation in the technic that I should like to mention. In a certain number of patients, multiparas more often than primiparas, labor begins with a sudden onset, the uterine contractions being strong and frequent. Early admittance of the patient with this type of labor into the hospital is urged. Frequently, by the time the patient has been prepared for the paraldehyde-benzyl alcohol instillation, labor has become quite painful. To these patients, the morphine sulphate is given at the same time as the rectal instillation, or in some cases, 15 to 20 minutes before. Often this will give a smoother and quicker induction to the analgesia and amnesia desired.

ILLUSTRATIVE CASE

Mrs. V. C., a 31-year-old primipara, weighing 146 pounds, was admitted to Garfield Memorial Hospital (case No. 122689) in early labor at 3:40 A.M. on November 16, 1936. Uterine contractions were occurring every 15 minutes, each lasting 40 seconds. She was given the usual preparations, including a thorough cleansing of the lower bowel. At 6:30 A.M. contractions were painful, coming every 6 to 8 minutes, and lasting 45 seconds each. Sterile vaginal examination revealed a cervix 3 cm. dilated, thick, soft, and one half effaced, the head beginning to engage. The first rectal injection of paraldehyde (18 cc.) and benzyl alcohol (1.5 cc.) was given at this time. One half hour later, since the patient was not asleep, one fourth grain of morphine sulphate was given. Contractions were now stronger, but 8 to 10 minutes apart. From 7:10 A.M. to 10:30 A.M. the patient slept soundly, with pains every 8 to 10 minutes. About 11 A.M. she began to arouse slightly with her pains, but upon catheterization, 18 ounces of urine being obtained, she rested quietly until 2:30 P.M. Examination at this time revealed the cervix to be thinning, 4 cm. dilated, and the head engaging in the R.O.P. position. The membranes were ruptured artificially. The pains were harder, coming every 6 minutes, and the patient stirred with each contraction. She was given 8 ounces of orange juice, the lower bowel was irrigated with normal saline solution, and the rectal injection was repeated at 4 P.M. She was catheterized again at 4:15 P.M. and 10 ounces of urine obtained. The patient slept quietly from 4:30 to 7:30 P.M., the pains being harder and occurring every 4 to 5 minutes. At 8 P.M. the contractions were coming every 3 to 4 minutes, and the third rectal injection was given. She was catheterized at 10:15 P.M. and 10 ounces of urine obtained. She rested quietly until 1 A.M. on the seventeenth, the pains becoming harder and closer. The fourth injection was given at this time after irrigating the lower bowel, and after administering orange juice. The patient rested quietly until 8:30 A.M., when she began to move, with strong pains every 2 to 3 minutes. Examination revealed the head in high midpelvis, R.O.P. position, with a definite rim of cervix present. The fifth rectal injection was given at 9 A.M. From this time until 12 noon she rested fairly quietly between pains, which were strong, occurring every 2 to 3 minutes. At 12:32 P.M. the cervix was completely dilated, the head arrested in the R.O.T. diameter in midpelvis, and under ethylene-oxygen anesthesia the patient was delivered of a 7 pound, 4 ounce female infant by means of mid-forceps following manual rotation and a left mediolateral perineotomy. To briefly summarize this case, the analgesia and amnesia obtained were excellent. The patient received 5 rectal injections and a total of 90 cc. of paraldehyde in 29 hours, or 1 dose every 5 hours and 48 minutes. One dose of morphine sulphate was given. The subsequent course of the mother and infant was uneventful.

CONCLUSIONS

1. The administration of paraldehyde and benzyl alcohol per rectum by the Kane-Roth method offers a safe and effectual method of alleviating the sufferings during parturition.

2. The technic is described in detail and a typical case reported.

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Fleas, Ticks, and Lice Retain Plague Infection After 10 Months in Ice Box.—According to a report dated August 9, 1937, from Dr. W. M. Dickie, Director of Public Health of California, specimens of fleas, ticks, and lice, taken from ground squirrels (*beecheyi*) in San Mateo County during September, 1936, and stored in the ice box until July of this year, produced typical plague infection when inoculated into guinea pigs. The following lots, all collected on September 25, 1936, were proved positive by guinea-pig inoculation:

15 fleas and 3 ticks from 1 *beecheyi* squirrel.
1 tick, 61 fleas, and 11 lice from 2 *beecheyi* squirrels.
36 lice and 24 fleas from 1 *beecheyi* squirrel.
29 fleas and 4 lice from 2 *beecheyi* squirrels.
31 fleas and 11 lice from 1 *beecheyi* squirrel.

All of the examinations were made by Dr. K. F. Meyer, Director of the Hooper Foundation for Medical Research.

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PROBABLE BACTERIAL ENDOCARDITIS APPARENTLY CURED WITH SULPHANILAMIDE

REPORT OF A CASE

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The following case of acute Streptococcus hemolyticus septicemia treated with sulphanilamide is reported because the use of this drug resulted in cure of the septicemia, because the possibility exists that the focus for the septicemia was an acute bacterial endocarditis, and because it is felt that the record of such cases in the literature is necessary for an accurate evaluation of this relatively new form of therapy.

Report of Case

M. B., a 34-year-old white man, was admitted to the Gallinger Municipal Hospital on May 14, 1937. At that time he had been ill 1 week with pain in the left gluteal region and afternoon fever. The pain was moderately intense and radiated down the posterior aspect of the thigh. It was not aggravated by movement. The fever had not been more than 101°F. on any day. The past history was negative except for frequent sore throats during the colder months of the year. There had been periodic excessive use of alcohol for about 10 years. The systemic history was negative except for slight loss of weight and constipation during the present illness. Family history revealed that the patient's mother died of heart disease at the age of 57 years. One brother, who is living, is known to have heart disease.

The patient was well developed and fairly well nourished. His skin and mucous membranes were moderately pale. He did not appear seriously ill. The tongue was slightly coated, many teeth were carious, and the nasopharynx was congested. The head and neck were otherwise negative. The lungs were negative except for scattered musical râles. The heart did not appear enlarged. The apex beat was in the fifth left intercostal space at the midclavicular line. There was a strong systolic thrill over the second right intercostal space near the sternum. A loud, harsh systolic murmur was heard in this same area. It had the usual transmission into the cervical vessels of the murmur of aortic stenosis. A softer systolic murmur was heard at the apex, transmitted to the axilla. No second sound could be heard in the aortic area. The cardiac rhythm was normal and the rate 80 per minute. The arterial blood pressure was 80 mm. Hg. systolic, and 58 diastolic. The abdomen, genitalia and rectum were normal. Extremities were negative except for tenderness on deep pressure over the left gluteal region. The deep tendon reflexes were equal and normal. The temperature 101°F.

With these findings the following impressions were recorded: (1) Rheumatic heart disease with aortic stenosis, (2) subacute bacterial endocarditis, (3) sciatica.

During the first 4 days in the hospital the patient did not appear gravely ill. His temperature varied between normal and 99.6°F. Preliminary laboratory studies showed the urine to be normal except for a moderate number of leukocytes. The hemoglobin was 80 per cent (Tallqvist); the white blood cells numbered 9,500 per cu. mm., of which 29 per cent were lymphocytes, 4 per cent large mononuclears, 14 per cent band forms, and 53 per cent mature granulocytes. The blood Kahn reaction was negative. A blood culture made on the third day yielded no growth. The physical findings did not change. Roentgen-ray examination of the chest was negative except for enlargement of the hilus glands on both sides; the heart was not enlarged.

On the fifth hospital day the patient appeared alarmingly ill for the first time. His temperature rose to 103.6°F. in the afternoon. The breathing grew labored and the pulse rate rapid. There was a severe chill. During the next 6 days his condition became progressively more grave. The temperature varied between 98°F. and 105.4°F. He suffered daily chills. A blood culture on the sixth hospital day was sterile, but cultures made on the eighth and tenth days yielded hemolytic streptococci. With this finding the diagnosis was changed as follows: (1) Streptococcus hemolyticus septicemia, (2) rheumatic heart disease with aortic stenosis and probable mitral stenosis, (3) possible acute bacterial endocarditis.

The murmur audible in the aortic area acquired a diastolic phase. The spleen became palpable on deep inspiration. The hemoglobin was 62 per cent (Newcomer), with 3,960,000 red blood corpuscles per cu. mm. on the seventh day. The urine remained the same as before.

On the eleventh hospital day administration of sulphanilamide was started. Twenty grains were given orally every 4 hours (80 grains daily). On the twelfth and thirteenth days the temperature did not rise above 102°F. By this time the patient was cyanotic from the sulphanilamide. He remained so until administration of the drug was stopped 25 days after it was started. In the following 2 weeks he appeared to grow steadily worse. His temperature ranged between 97°F. and 102°F. with corresponding fluctuation of the pulse rate. Supportive treatment was used in the form of intravenous infusions of 5 per cent glucose solution (2,000 cc. daily) and repeated small transfusions of blood. In spite of these transfusions the anemia became more severe, the hemoglobin falling as low as 47.5 per cent (Newcomer). The white blood cell count reached a peak of 22,500 per cu. mm. on the twenty-fifth day.

From the ninth to the twentieth hospital day the patient complained of pain in the left lower extremity. Moderate edema and slight redness were present. This was believed to be due to acute thrombophlebitis. After the twentieth day it gradually subsided. Fluoroscopic examination of the chest on the twelfth day showed no change from the previous roentgen-ray examination.

On the twenty-sixth day, when the prognosis had come to appear hopeless, the patient's temperature dropped to normal and stayed there except on 2 occasions, following blood transfusions. His toxemia disappeared quickly, and he improved subjectively. Administration of sulphanilamide was continued for 10 days after the patient's temperature became normal. During this time the spleen diminished in size until it could no longer be felt and the white blood cell count returned to normal. Several blood cultures yielded no organisms.

The patient remained in the hospital nearly 4 weeks after administration of sulphanilamide was stopped. During this time he had a convalescence resembling that of a patient recovering from a severe acute illness, such as lobar pneumonia. He was discharged from the hospital on July 17, 1937. By this time he felt well and had no important abnormalities on examination, except that the cardiac findings were the same as at the time of admission. He was reëxamined on July 29, 1937, when there were no new findings except moderate postural dependent edema of the left leg.

Comment

The use of sulphanilamide in the treatment of this patient apparently cured his septicemia. Perhaps more scientific importance might be attached to this result if it were certain that the focus for the septicemia was in the endocardium. Strongly in favor of the impression of bacterial endocarditis were the cardiac findings, particularly the development of an aortic diastolic murmur during the course of the illness, and the splenomegaly. Against the impression was the absence of embolic manifestations. Certainly, in view of the absence of other cause for the septicemia and in view of the clinical picture, it is probable that bacterial endocarditis existed. It should be noted that the sulphanilamide was used in large doses for a long time in spite of cyanosis and without deleterious effect. Had it been discontinued after the usual trial period or because of the cyanosis it is possible that the patient would not have recovered.

LEARNING-DISABILITY IN INTELLIGENT CHILDREN—A SYMPTOM OF EMOTIONAL DISTURBANCE*

Agnes B. Greig, M.D.
Washington

In the brief time at my disposal it is impossible to go deeply into any psychiatric problem or to present a comprehensive piece of research, but I would like to present a thought from my special field of child psychiatry which would be of general interest and perhaps bring a measure of awareness to an every-day situation which is not generally recognized but which can be of grave significance.

Intelligence is defined as the ability to learn, and the problem which I wish to bring to your attention is that of the child who has the ability to learn but who in actual fact does not learn.

In the first place one has to decide whether he really has the ability to learn. If the child is actually developing up to his capacity it is essential to his well-being that he be not pushed, or there will be trouble.

The two pictures may be similar, i.e., that of the slow child who is protesting against being pushed and that of the child with potential ability which is suppressed. Both will show signs of stress which may take many forms.

Intelligence tests are very valuable if we accept them for what they are worth and do not endow them with magical qualities. Aptly applied, they tell us what they were intended to tell us, namely, the child's functioning intelligence but not his potential intelligence.

The child has tremendous ability to cover up or camouflage his fears, and his symptoms very frequently appear to be too remote to suggest any connection with the real trouble.

If a child who has been developing rapidly and making good progress in his school work becomes inattentive and makes poor grades it is easy to see that he is not learning up to his normal capacity; but there is little appreciation of the fact that he is for the time-being unable to learn, and he is constantly scolded and prodded to do what everyone is so sure he is capable of doing. The intelligent educator is becoming increasingly aware of the fact that the child is suffering from some emotional conflict, but he apparently does not know that he is not just thinking of something else, that even when he is not consciously thinking of anything but his lessons he is unable to learn, that he is unable to function efficiently in any direction, that his mental illness is to a certain degree paralyzing him.

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* Read at the Annual Scientific Assembly of the Society, May 5, 1937.

It is this symptom of emotional conflict, this paralyzing force, which I wish to stress.

But, serious as the above may be, there is no question of lack of inherent ability. However, such a state of paralysis in varying degree is not infrequently present in the child at the beginning of his school career or develops at the beginning.

The cause can invariably be traced back to fear of a lack within himself to cope with the situation in hand. He may be likened to the turtle who at the first sign of danger draws back into his shell and will venture forth only when the threat seems removed. We realize that no amount of threat or prodding will bring him forth, but with children we do just that. Perhaps if the child, too, carried a visible shell we would try the only method which ever does work, i.e., provide him with security—freedom from the threat of danger or the weapons with which to overcome it—instead of using all our energies in driving him back to cover where he cannot develop any potential powers which he may have but to which such imprisonment can bring only death.

What may give rise to such fear in a child?

Childhood is a strenuous battle. From the beginning he is forced to defer and modify the gratification of instinctual needs, and each new adjustment is fraught with anxiety. He is hungry, but it is not feeding time—perhaps food will never come. He is lonely—perhaps mother will never return. Very early he learns the pain of disapproval. How delightful and satisfactory are his bodily functions and the interest in his own person, but grownups with their imponderable ways say, "dirty," "naughty," and show disgust and repugnance. This creates tremendous anxiety. Love, which to the child means security, must be won at any price but how may he come to know what will please and what will bring punishment? Much creative impulse must be checked by this anxiety, since creative freedom can exist only in an atmosphere of peace. Any new venture is met with this anxiety. If it is not too great and one ventures cautiously and meets with success and approval, there is a great release of energies. If, however, one is met with failure and disfavor, one retreats.

When the individual has met with a reasonable measure of success he can stand more failures because he has the supporting force of the past success; but the child who has not yet had time to build up a past and has only the present is highly vulnerable, and total defeat robs him of the vital force necessary for success.

School is one of the big milestones, and there are many chances of failure there.

Our competitive mode of life tends to make us measure children by a common yardstick. The standard adopted must be one which can be given form, rigidity. Hence the tangible intellectual abilities are made the criterion, and the intelligence tests which were designed to aid in grouping children to their advantage are commonly made to cover the total personality, with a fine disregard for emotional values.

Intellectual pursuits are essentially escapes from real emotions, and many children who make rapid progress in their studies and who are rated superior children to the detriment of their less intellectually keen fellows are actually retreating from life; and although they are able with great rapidity to follow in the footsteps of great leaders who may themselves be vastly creative, they themselves can rarely blaze new trails.

On the other hand, many children who have greater emotional freedom and consequently stronger creative urges do not have the same eagerness for intellectual pursuits, and if a trauma is sustained their escape is more likely to be away from, rather than into, the realm of the intellect.

I shall briefly present 2 cases which illustrate my point. They are of necessity very sketchy, and many important features are omitted.

Case 1: Jane, aged 8 years and 2 months, was disobedient and lacked sustained interests. She had been 1 year in kindergarten, 1½ years in first grade, and was promoted to the "slow" second grade because she was large and the school hoped the promotion would stimulate her to better work, but her failures were increasing. Her behavior was described as silly, uncoöperative and annoying to the other children. She was thoroughly unpopular with children and teachers. At her first interview she gave the impression both in appearance and behavior of a definitely subnormal child, and only after a number of interviews of 1 hour's duration each did she begin to show other possibilities. She was the younger of 2 children, the older being 3 years her senior and from the history well adjusted at home and at school. Both parents were highly intelligent and intellectually ambitious. The mother was an intensely competitive person, and from infancy Jane showed the strain by excessive irritability and a reluctance to attempt anything new. She had practically no playmates until she was 4 years old, at which time a very aggressive 4-year-old girl moved next door. She was a very poor companion for Jane, since her overassurance further intimidated my patient. Nevertheless, there was considerable happiness in the relationship, and on Jane's part abject devotion, until the group enlarged. Then the neighbor child used her power over Jane as a very cruel weapon, playing with her when it pleased her to do so and at other times deserting her heartlessly, and as a leader of the group frequently humiliating Jane, who was large and a little clumsy, before the others. When Jane started to school she was confronted with a terrifying new world, the most terrifying part of it being the large group of children. From the start she suffered from a mental paralysis. Psychotherapy applied to the family situation as well as to the child relieved much strain, and Jane's removal from the school and placement with a small ungraded group and understanding teacher literally transformed her. In 1½ years in the small group and with a little tutoring combined with an active country life during the summer, she had not only caught up with, but had gone a little beyond her age group and was able to enter public school in a new neighborhood, where she is now continuing to be happy and successful, both socially and scholastically.

Case 2: Robert, aged 7 years, had been stealing and failed in school. He had completed almost a full year in first grade but showed no evidence of having learned anything. Achievement tests rated him subnormal. His father was convinced he was feeble-minded. His mother was worried but wanted to believe there was some other explanation. However, the fact remained he had not learned to read and could make nothing of arithmetic, although he did appear to try.

The situation was found to be as follows: Up to the age of 20 months he was a "sunny," healthy child who showed every evidence of developing normally both physically and mentally. A baby sister arrived and was very joyously received. Robert began to be excessively destructive, but because of his obvious devotion to his little sister it didn't seem to suggest jealousy. At 3 years he began stealing small articles, such as cuff links, rings, money, watches, etc. As his mother expressed it, they never seemed able to teach him the difference between mine and thine. He played well with younger children and was a favorite with adults, but had no playmates of his own age until he entered school. He appeared to adjust fairly well, but outside of school his preference was for younger children, and the stealing steadily increased. He tried pathetically hard but never seemed able to retain anything. Psychiatric examination revealed intense jealousy of the clever little sister and strong feeling of personal inadequacy for additional reasons which I cannot go into. It seemed wise to remove him from school entirely for a time. His response to psychotherapy was such that he was able the following year to enter public school, but a different one because of the associations, and during these past 4 years he has had no difficulty in keeping up with his grades, is well adjusted to his own age group and shows every indication of having ahead of him a normal, well-rounded life. Incidentally, there has been no more stealing.

These cases are of necessity very incomplete, and the point I stress is only one of many symptoms; but there is need for a greater realization of the fact that during emotional conflicts minds are crippled, and it is just as serious to ignore this fact as it would be to ignore the fact that during a serious illness the child cannot, and must not be forced into attempting to lead a normal, active life.

Fortunately, the mind, like the body, has tremendous adaptive and recuperative powers, but it is just as hazardous to leave these mental ills untreated as to leave the child with, let us say, an untreated fracture. The chances are very good that it will heal, but the chances are also very good that very serious limitations of function will result.

A Complication of Injection Treatment of Hernia.—*Case Report.*—J. J. M., a 62-year-old, white, married man (Faulkner Hospital No. 47331), was first seen at his home March 15, 1937. About 2 hours after dinner he had begun to have cramp-like pains in the abdomen, which started in the left lower quadrant, radiated up the left side and ended in the midline between the epigastrium and the umbilicus. He had never had previous pain of this type. He stated that he had had a "lump" in his right side for a considerable period of time but that he could not afford an operation, and therefore went to a clinic and had his hernia injected. He had had 17 injections, the last one being 5 weeks previously. When the series was completed the "lump" in the side had disappeared. . . . . .

In the hospital a barium enema showed no obstruction in the colon. Small amounts of barium were given by mouth and were followed by X-ray plates and fluoroscopic examination. Neither was very satisfactory, failing to reveal any pathology but showing a large amount of gas in the small bowel. The symptoms of pain and vomiting continued for 3 days, and the pain did not shift from its original location. . . . . .

. . . . . . The preoperative diagnosis was partial small bowel obstruction due to adhesions as a result of hernial injections.

Under spinal anesthesia a right paramedian incision was made. When the peritoneal cavity was opened there was a moderate amount of free fluid. On inspection a loop of dilated small bowel and also collapsed small bowel were seen in the right lower quadrant. Tracing this condition distally there was found an obstruction in the small bowel due to an adhesion which drew the bowel up and attached it to the abdominal wall at the site of the internal inguinal ring. The bowel was constricted to about two thirds of its original size, and for about 5 cm. on either side of this constriction the musculature was greatly thickened. The adhesion was divided close to the abdominal wall at the internal ring. A second adhesion which connected loops of bowel one with another and attached them lower down to the abdominal wall below the internal ring was also separated. . . . . . Two hundred cubic centimeters of amfetin was put into the abdominal cavity before closing. An appendectomy was also done.

Conclusion.—Injection treatment of hernia may have, as one of its complications, intestinal obstruction due to adhesions around the bowel which have resulted from the entrance of the sclerosing solution into the peritoneal cavity.

Abstract from article by EUGENE F. McDONOUGH, M.D., West Roxbury, Mass., *New England Journal of Medicine, September 2, 1937. p. 402.*

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THE HEALTH DEPARTMENT'S AMBITIONS

Every member of the Medical Society of the District of Columbia, as well as every citizen of the District, can enthusiastically support the Health Officer in his efforts to reduce mortality and morbidity due to disease. The death rate in the District of Columbia is far too high. The main reason for this undoubtedly is inability to carry out a well-organized preventive disease program because of lack of sufficient funds. Now that taxes have been raised and it appears more probable that the Health Officer will be able to secure a larger appropriation for the work of his Department, and since he has asked for an increase of 54 per cent in his budget for 1938, careful scrutiny is in order to ascertain how the greatest results can be obtained.

First, it would appear that better use could be made of already existing resources for the care of the underprivileged sick. There have existed in the District of Columbia for many years several large free polyclinics in large community hospitals, namely, Providence Hospital, Emergency Hospital, Children's Hospital, Garfield Memorial Hospital, Georgetown University Hospital, and George Washington University Hospital. Many thousands of ambulatory patients have been treated each year in these clinics without support from the District Government. Many of the physicians working in these clinics without remuneration are well trained, and examinations and treatment are of a high order of efficiency. All types of diseases are treated in these clinics. It would appear logical that the Health Officer should become familiar with all of these facilities and services, should attempt to secure the confidence and coöperation of the staffs, and should make serious efforts to amalgamate these clinics with his Department without destroying their individuality. There should be one main system of preventive and curative medicine composed of well-integrated units. Centralization of pertinent data of patients and of social service follow-up should be developed. In this way greater efficiency of each unit and of the whole and a smaller total expenditure of public funds would be assured. Proper approach would undoubtedly result in wholehearted coöperation along these lines. Among others the venereal disease problem could be much better solved.

Secondly, one of the greatest sources of wasted efforts in connection with indigent patients requiring hospitalization is an almost total lack of social service follow-up. This means that after being discharged from municipal hospitals many patients requiring home treatment become careless in following directions of hospital physicians or do not understand sufficiently what they are supposed to do. Many are advised to attend outpatient clinics but fail to do so. Consequently frequent relapses and recurrences of disease occur and hospitalization is again required. Such repeated and often unnecessary periods of hospitalization are very expensive to the taxpayers. An adequate social service department would actually be less expensive.

Thirdly, there is a great problem in connection with the domiciliary care of the indigent sick. At present many patients are hospitalized at considerable expense who could be treated at home if physicians were available for this type of work. The small number of underpaid Physicians to the Poor is entirely inadequate. Great progress in this field would result if medical students were used for this purpose. There are 3 medical schools in the District of Columbia. The medical students examine and treat patients under supervision in the outpatient departments of community hospitals and in the wards of community and municipal hospitals, but except in the case of obstetrical patients they do not visit patients in their homes. For several years one medical school has maintained a very satisfactory service for home obstetrics. Medical students under adequate supervision of obstetricians treat many obstetrical patients in their homes. It would be quite possible to institute similar services for other classes of patients. Senior students could be assigned to this work under supervision of the physicians of the Health Department. In this way the students would profit greatly by more adequate training, expensive hospitalization would often be obviated, and the objectives of the Health Department would be furthered.

The above constructive suggestions are made purely with the motive of hoping to aid the Health Officer to solve his many problems and to attain the ends that all desire him to achieve. These ends should be gained economically, if possible. The plans suggested would not only make for greater efficiency but for economy. They would also help to make a great many individuals more interested in public health work and would tend toward the ideal of "every physician a health officer."

ARE THE HOSPITALS BROAD-MINDED?

The Hospital Superintendents' Association has recently requested the Central Admitting Bureau for Hospitals to practically sever its connection with the Medical-Dental Service Bureau by withdrawing its collection accounts from that organization. This would seriously affect the Medical-Dental Service Bureau, disrupting a predetermined policy that has proved its value to the hospitals, to the public, and to the profession.

The Central Admitting Bureau for Hospitals was established as a clearing house for the underprivileged sick and as a disbursing agency for Community Chest contributions to the hospitals. It was early decided to have the Medical-Dental Service Bureau collect the money promised by the patients to make up the balance of the $4.00 per diem for hospitalization at a 10 per cent commission. This Bureau has done this job satisfactorily and with the minimum of cost. It is safe to state that no other agency could do it more cheaply. However, because the hospital superintendents have without foundation in fact developed a theory that these collections could be made more cheaply they are planning to take this function away from the Medical-Dental Service Bureau and give it to the Central Admitting Bureau for Hospitals.

Now, largely because of this business and the fact that the two bureaus shared overhead expenses the Medical-Dental Service Bureau has been enabled to keep growing and to exist at very little expense, so that for nearly a year under its present management its income has been upwards of $200.00 per month more than its expenses. After all debts are paid it was planned that this excess would go into a sinking fund to aid semi-indigent patients to secure medical and dental care and hospitalization without loss of their self-respect by becoming wards of the state. If the Medical-Dental Service Bureau is made to give up this function and to move its offices it would jeopardize this and other objectives which were contemplated for the amelioration of problems confronting the sick.

The Medical-Dental Service Bureau has always paid more than its share toward the rent, upkeep and telephone service of the Health Security Building at Eighth and Eye Streets, where these Bureaus together with the Permit Bureau of the Health Department are housed. Nevertheless the hospital superintendents believe the Central Admitting Bureau for Hospitals could do the job more cheaply, apparently forgetting that that Bureau would need just as much space, just as many people, just as much telephone service and just as much equipment as the Medical-Dental Service Bureau. Any advantage to be gained by the hospitals through the change is very doubtful.

Furthermore, the hospital superintendents have apparently forgotten that both the Central Admitting Bureau for Hospitals and the Medical-Dental Service Bureau were developed and have been continuously fostered by the organized medical and dental professions of the District of Columbia as part of the Health Security Administration of the District of Columbia for the express purpose of helping people of small means obtain adequate medical and dental care according to their ability to pay. The Medical-Dental Service Bureau is incorporated. Four organizations of professional men and women, to wit, the Medical Society of the District of Columbia, the District of Columbia Dental Society, the Medico-Chirurgical Society, and the Robert T. Freeman Dental Society, contributed from their respective funds loans without interest in good faith to make the venture possible. Although some return has been made, there is still a considerable balance on the loans remaining due and payable. The corporation has equipment, including bookkeeping machines, cash registers, and other office labor-saving devices, worth hundreds of dollars, most of which are paid for in full; a setup ready to carry on economically and effectively. The Central Admitting Bureau for Hospitals possesses none of these facilities. The responsibilities and implications in making an equitable adjustment of property rights of the corporation and of the various societies are apparent and definitely inherent in the fostering of a plan such as proposed by the hospitals. Without any consideration for the wishes of physicians and dentists and without manifesting any interest in the big community problems involved the superintendents have dogmatically demanded what amounts to destruction of a very important part of the plan and a transference of a function to an organization ill suited—not at all equipped.

The hospital superintendents have also apparently forgotten that hospitals exist so that physicians may take better care of the sick. That some dissatisfaction exists with the way hospitals are run is indicated by plans for the establishment of a new hospital to be run by physicians. To have the hospitals disregard the physicians as they are doing in the present stance is somewhat like "the tail wagging the dog."

It is hoped that a contemplated conference between representatives of the Board of Directors of the Central Admitting Bureau for Hospitals and the Medical-Dental Service Bureau will bring a solution whereby both organizations may serve the public in the manner originally intended.

COMING MEETINGS

Wednesday, October 6: Business Meeting. Reports of Committees, etc.

Wednesday, October 13:

The Davidson Lecture.

"Factors in the Production and Treatment of Shock: An Experimental Study." Harry A. Davis, M.D., C.M.

Buffet Supper.

Wednesday, October 20:

1. "Jaundice: Its Clinical Interpretation." William J. Mallory, M.D.
2. "Reduction of Gallbladder Mortality." J. Russell Verbrycke, Jr., M.D.

Wednesday, October 27:

1. "Statistical Survey of Pulmonary Tuberculosis in the Nation's Capital for the Past Ten Years with an Interpretation of the Problem Revealed." George C. Ruhland, M.D., and C. C. Dauer, M.D., Health Department.
2. "Practical Clinical Considerations in the Diagnosis, Prognosis, and Treatment of Pulmonary Tuberculosis." Samuel Wolman, M.D., Baltimore, Md.

DAVIDSON LECTURE

Biennially a lecturer is selected to deliver before the Society a scientific treatise on a topic dealing with products of his own research. Established in 1929, in commemoration of the outstanding service rendered the Washington profession by Dr. Edward Young Davidson, more and more have these lectures attracted national attention. Heretofore, outstanding men of wide-spread recognition have been invited to make the address. In 1936 the Executive Committee adopted a resolution to put the selection of the lecturer on a competitive basis. The Davidson Lecture, it was believed, should mean more than the opportunity of hearing a paper prepared by the hand of some great master. It should be a stimulus to local talent especially the younger men to higher performance. It was accordingly agreed that "the selection of the Davidson Lecturer shall be on the basis of competition, the winning essay to be selected by a subcommittee consisting of five (5) members of the Executive Committee appointed by the Chairman. . . ." The second

Wednesday in October of odd numbered years was fixed as the permanent date. Pursuant to this, the Committee, as a result of its deliberations, has recently announced that Dr. Harry A. Davis' paper, entitled "Factors in the Production and Treatment of Shock: An Experimental Study," was deemed the most suitable of the papers which were submitted following the well-publicized announcement of the contest. The personnel of the Committee on Selection of Essayist included: Drs. F. X. McGovern, Chairman; A. J. B. Connolly, Raymond T. Holden, Jr., Oscar B. Hunter, and Coursen B. Conklin. The following criteria for judging papers were used:

I. Subject: Appeal to general interest of members.
II. Content: 1. Arrangement, inclusive of outline.
    2. Length.
    3. Relationship of (a) Data derived from personal research.
        (b) Data derived from literature.
    4. Conclusions.
III. Value or possibilities of whole as a contribution toward advancement of medicine.

It was indeed gratifying to receive the response from the local physicians, to know that there is going on scientific work of such importance, most of it without the advantages of endowment. It was no easy task for the Committee to rate the products of investigation submitted. Dr. Davis well deserves the congratulations of the membership. A large attendance will be an expression of appreciation not only to the essayist but to Dr. Edward Young Davidson who made our present building with its facilities possible.

To the meeting on October 13, members should invite their medical friends of the environs of Washington. These lectures should continue to take a prominent place on Washington's Medical Calendar and should fully exemplify the spirit of service which actuated their inception.

Dr. Harry Aaron Davis, until recently Instructor in Pathology, George Washington University School of Medicine, now Associate in Pathology, University of Tennessee School of Medicine, was born in London, England, September 27, 1905. During early infancy he was taken by his parents to Edinburgh, where he later received his preliminary education in the Royal High School. He successively became, in 1928, a Licentiate of the Royal College of Physicians of Edinburgh, of the Royal College of Surgeons of Edinburgh, and of the Royal Faculty of Physicians and Surgeons of Glasgow. He attended the University of Edinburgh for a period of 6 years. In 1931 he was graduated from McGill University, Canada; becoming in 1935 a licentiate of the National Board of Medical Examiners. He obtained a Fellowship in Surgery at the Mayo Clinic while working at McGill University. He then successively became a Koessler Fellow in Experimental Surgery, 1933–1935; Instructor in Pathology, George Washington University School of Medicine, 1935–1937; and recently Associate Professor of Pathology, University of Tennessee School of Medicine in 1937. Among his published papers are noted:

Harry Aaron Davis, M.D., C.M.
The Davidson Lecturer, 1937

Congenitally Ectopic Uterus in Sac of Inguinal Hernia. (With Counsellor, V. S.) S. Clin. North America, 1932, 12, 1039.

The Behavior of Isotonic and Hypertonic Solutions in the Blood Stream of Normal and Dehydrated Animals. Proc. Soc. Exper. Biol. & Med., 1934, 32, 210.

Studies in Water Balance. I. Excessive Oxygen Usage Response of Dehydrated Animals to Water and Electrolytes. Ibid., 1935, 33, 242.

Studies in Water Balance: II. Anoxemia Factor in Water Intoxication. Ibid., 1935, 33, 245.

The Relation of Water and Electrolytes to Metabolism. Science, 1935, **81**, 493.

The Relative Significance of Electrolyte Concentration and Tissue Reaction in Water Metabolism. (With Dragstedt, L. R.) Am. J. Physiol., 1935, **113**, 193.

Influence of Water Administration Upon Oxygen Consumption Rate in Shock. Proc. Soc. Exper. Biol. & Med., 1936, **34**, 21.

Physiologic Availability of Fluids in Secondary Shock. Arch. Surg., 1937, **35**, 461.

NEWS AND PERSONALS

The Woman's Auxiliary to the Medical Society of the District of Columbia. Results of election of officers, held on May 25, 1937:

Mrs. Thomas E. Neill, *President*
Mrs. Raymond T. Holden, *First Vice President*
Mrs. James G. Cumming, *Second Vice President*
Mrs. Harry F. Anderson, *Treasurer*
Mrs. Robert M. Bolton, *Corresponding Secretary*
Mrs. Beveridge Miller, *Recording Secretary*
Mrs. C. N. Chipman, *Historian*

American Association for the Study of Neoplastic Diseases met at the Mayflower Hotel, September 9–11, 1937. Participants from the Medical Society of the District of Columbia presented the following:

"Lymphosarcoma of the Stomach," also "The Nature of Certain Kidney Tumors." Eugene R. Whitmore, M.D.
"Non-industrial Tumors of the Bladder." R. M. LeComte, M.D.
"Teratoma of the Testis." Janvier W. Lindsay, M.D.
Dr Ramsey Spillman, a former member now located in New York City, demonstrated "Trauma in Bone Sarcoma."

Dr. Eugene R. Whitmore, of Washington, is the present Secretary; Dr. George A. Stewart, of Baltimore, President.

Fifth International Congress of Radiology, Palmer House, Chicago, September 12–17, 1937, Arthur C. Christie, M.D., President. Participants from the Medical Society of the District of Columbia:

"Motion in the Vertebral Column." Joseph F. Elward, M.D.
"Treatment of Female Endocrinopathies." Jacob Kotz, M.D., and Elizabeth Parker, M.D.
"Special Problems of Radiation Therapy Relating Particularly to Treatment of Cancer of the Cervix and Cancer of the Breast." Edwin A. Merritt, M.D.

Health Department Laboratory Improves Service. Improvements in appearance, equipment and laboratory practices have been made in the laboratory. These changes, by no means extravagant, outshine any renovation of the interior or innovation of practice in the history of the laboratory. Except for one painting, no remodeling or interior changes have occurred in 20 years. A new refrigerator will insure the proper storage of vaccines, an important but much delayed improvement. The great volume of Wassermanns and Kahns due to the response of the public to the syphilis campaign overwhelmed the serological staff. Some additional personnel and equipment temporarily relieved the congestion. Dr. John E. Noble is the Director of the Bureau of Laboratories for the District of Columbia.

Release of the First Supplement to the U. S. P. XI. The Pharmacopoeial Convention of 1930 approved the following resolution which had been passed, in substantially the same form, by many preceding U. S. P. Conventions:

> "*Supplements*—It is recommended that the Committee of Revision be authorized to prepare supplements to the Pharmacopoeia, or lists of admissions or changes at any time they may deem such action desirable." (U. S. P. XI, page lxvi).

Under this authorization the U. S. P. Committee of Revision and Board of Trustees have prepared and published the First Supplement to the U. S. P. XI.

This First Supplement has just been released and will become official on December 1, 1937. It is a booklet of about 100 pages in a substantial binding and may be obtained from the Mack Printing Company, Easton, Penna., from your wholesale druggist, or from any other distributor of the U. S. P., at $1.00 per copy, postpaid. In this supplement all of the texts revised to June 1, 1937, are reprinted in full so that there can be no misunderstanding of the authorized changes.

The New Tuberculosis Sanatorium at Glenn Dale, Md., was opened formally for inspection on September 15. The dedicatory exercises were held at 2:30 P.M. Modern in every detail from culinary department to operating room this plant will stand as a model for some years to come. Among the unusual modern equipment are found an auditorium, with projection booths, available radio outlets, indirect lighting controllable by patient from low to brightest candle-power. The members of the Medical Society of the District of Columbia should indeed feel proud of this product of local effort in which they played no little part.

Drs. W. Calhoun Stirling and A. M. Lands were recently awarded a certificate of merit for the scientific exhibit which they presented, by invitation, before the Annual Meeting of the Medical Society of New Jersey. They were also invited to present their exhibit on kidney trauma before the National meeting of the Association of Military Surgeons of the United States, in Los Angeles, California, October 14–16, 1937, and before the Annual Graduate Fortnight of the New York Academy of Medicine in New York City in November.

George H. Simmons, M.D.

(1852–1937)

Dr. George H. Simmons, Editor and General Manager Emeritus of the Journal of the American Medical Association, died at Saint Luke's Hospital, Chicago, on September 1, 1937. He served during the period of greatest development in the American Medical Association, filling the position as General Secretary, 1899–1911, and of Editor, which he occupied until 1924. Upon his becoming General Manager in 1901 the business and professional affairs of the Association were, to say the least, disorganized. He had developed plans for reorganization through a committee of which Dr. J. N. McCormack of Kentucky was chairman and he secretary. The American Medical Association became the representative organization that it is today. Annual publication of ratings of medical schools, reports of the Council on Medical Education and Hospitals, Council on Pharmacy and Chemistry, and Department of Propaganda for Reform, which latter became eventually the Bureau of Investigation, began to appear in the pages of the Journal, American Medical Association, during his skilful editorship. The Quarterly Cumulative Index is but another item of service to physicians originally developed by Dr. Simmons. His attacks on quackery and fraud in the field of medicine brought attempts at reprisal from those who saw their unscrupulous exploitation exposed. Chronologically may be briefly summarized events in his early life:

Born in Moreton, England, January 2, 1852.

Came to the United States in 1870.

Attended Tabor College, Iowa, 1871–1872.

University of Nebraska, 1872–1876.

Hahnemann Medical College, Chicago, M.D., 1882.

Rush Medical College, M.D., in course, 1892.

Practiced in Lincoln, Nebraska, 1884–1899.

His literary career as Editor was developed in serving variously the Nebraska Farmer, Nebraska State Journal, Omaha Republican, the Kansas City Journal, and other publications.

With Dr. Simmons' passing, at the age of 85 years, an impress is left on American Medicine which is permanent and which gives to the American Medical Association its place of preëminence among other national organizations representing other countries. "The medical profession of the United States owes him a debt which it could never pay and which he never wished to collect."

Elijah Lumbia Mason, M.D.

(1871–1937)

Dr. E. L. Mason, a graduate of Columbian (now George Washington) University School of Medicine, in 1901, died on August 30, 1937, following long incapacity resulting from injuries received in a fall while attending patients. He became a member of the Medical Association of the District of Columbia on April 2, 1902, and of the Medical Society of the District of Columbia on October 1, 1902. Since entering the practice of medicine he continuously lived in Washington. Among his hospital appointments were included Garfield Memorial Hospital and Episcopal Eye, Ear and Throat Hospital. He was sometime pathologist and bacteriologist to Children's Hospital and visiting physician at Washington City Orphan Asylum. Dr. Mason was active in the work of the Hippocrates-Galen Society, at one time serving as President. Among his national society memberships were included Fellowship in the American Medical Association and the American College of Physicians.

Dr. Mason was born in Rocky Mount, Va., February 23, 1871, the son of Gilbert L. and Susan Floyd Mason. He is survived by his widow, Mrs. Viola Hines Mason, and a son, Jack Wellons Mason.

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THE DIAGNOSTIC VALUE OF THE BLOOD PHOSPHATASE DETERMINATION

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Phosphatase is an enzyme which has the capacity to hydrolyze monophosphoric esters. It appears that there is more than one phosphatase in mammalian tissues and the term as used has a somewhat general meaning, signifying an enzymic agent capable of splitting a monophosphoric ester. Thus far it has been shown that the phosphatases of bone, kidney and intestinal mucosa are capable of splitting 36 different monophosphoric esters. Phosphatases have been found in the following tissues or fluids: small intestine, colon, stomach, kidney, ossifying cartilage, bone, periosteum, teeth, spleen, liver, pancreas, lung, thyroid, thymus, urine, bile, blood plasma, red-blood cells and leukocytes (Cantarow).

The plasma phosphatase content of the tissues is highest in the young. It varies inversely with age until adult life is reached. With the Bodansky method the normal serum phosphatase for the adult varies from 1.5 to 4.0 units; for children, 2 to 15 years of age, the normal value ranges from 3.1 to 13.1 units (Bodansky and Jaffe).

The phosphatase content of blood is influenced by the diet and the state of nutrition. Bodansky has shown that the phosphatase content of blood serum is decreased by prolonged fasting and by protein (meat) feeding, is increased by the ingestion of carbohydrates and is not affected by fat ingestion. It has been observed that the serum phosphatase content is low in cachexia and malnutrition.

An increase in the phosphatase of blood plasma is interpreted as being due to physiological or pathologic overproduction of phosphatase in the tissues known to contain phosphatase and a resulting overflow of the enzyme from the site of production. Normal increases in plasma phosphatase, e.g., following carbohydrate ingestion, probably result from increased production by the intestinal mucosa or the liver. It has been suggested that the kidneys phosphorylate glucose in the tubular epithelium as a preliminary to glucose reabsorption (Lundsgaard); if this interesting hypothesis is true, it may be essential for the kidneys to produce phosphatase. Increases in plasma phosphatase in bone disease are undoubtedly of osseous origin; and the increases in biliary obstruction or liver diseases may be of hepatogenous origin.

Phosphatase participates actively in the formation of bone. This enzyme hydrolyzes phosphoric esters in zones of ossification, creating a local excess of phosphate ions, which in the presence of calcium ions results in the deposition of tricalcium phosphate because the solubility product of the latter substance is exceeded (Kay).

In conditions in which there is active new bone formation there is an unusual outpouring of phosphatase from the centers of rapid ossification into the blood stream. The phosphatase activity of the blood plasma is thus increased as a result of new bone formation and may be taken as a measure of the rate of osteogenesis.

The determination of the serum or plasma phosphatase is, therefore, a valuable laboratory test in the examination of lesions of the bones.

BLOOD PHOSPHATASE IN LESIONS OF THE BONES

The phosphatase activity of blood plasma is increased in the osteoblastic type of osteogenic sarcoma, in osteitis deformans (Paget's disease of bone), in hyperparathyroidism (generalized osteitis fibrosa cystica; von Recklinghausen's disease of bone), and in rickets. The diagnostic significance of plasma phosphatase in bone conditions may be summarized as follows:

1. *Malignant tumors primary in bone.* In osteogenic sarcoma of the osteoblastic type the plasma phosphatase is high. In the osteolytic type of osteogenic sarcoma, in multiple myeloma, endothelial myeloma, chondroma, and chondrosarcoma, the phosphatase is normal or only slightly increased (Bodansky and Jaffe; Franseen and McLean; Simmons and Franseen; Woodard, Twombly and Coley).

2. *Tumors with metastases to bone.* In cases of malignant tumors not primary in bone but with metastases to bone there may be an increase in the plasma phosphatase (Simmons and Franseen; Woodard, Twombly and Coley; Roe and Whitmore). When the bone lesions are small or osteolytic in type, there is little or no increase in phosphatase; osteoblastic metastases, on the other hand, as in most prostatic cancers and in some metastases of mammary cancer to bone, are associated with high plasma phosphatase. There is no increase in phosphatase in carcinoma with metastases other than to bone.

3. *Osteitis deformans and generalized osteitis fibrosa cystica.* The blood plasma phosphatase is very high in osteitis deformans (Bodansky and Jaffe; Kay; Franseen and McLean; Simmons and Franseen; Woodard, Twombly and Coley; Roe and Whitmore). In osteitis fibrosa cystica there is a characteristic increase in blood phosphatase, but the activity is much less than occurs in osteitis deformans. The usual picture of hyperparathyroidism is a high calcium, low phosphorus and a moderately increased phosphatase activity of the blood.

4. *Tumors without bone involvement and benign tumors of bone.* The blood plasma phosphatase is not increased in such lesions (Bodansky and Jaffe; Woodard, Twombly and Coley; Roe and Whitmore).

5. *Rickets.* The plasma phosphatase is high in rickets (Bodansky and Jaffe; Kay; Simmons and Franseen). This has been explained as "frustrated attempts at osteogenesis." There is increased osteoid tissue with increases in phosphatase which are apparently compensatory attempts to lay down bone. The blood phosphatase activity is regarded as a reliable criterion of the severity of rickets and may be of value in following the results of therapy.

6. *Fractures.* There is an increase in plasma phosphatase in healing fractures during the period of increased osteoblastic activity (Bodansky and Jaffe).

7. *Osteomyelitis.* When there is little regeneration of bone in osteomyelitis, the plasma phosphatase tends to be normal. A moderate rise may occur in an acute or an extensive lesion (Bodansky and Jaffe; Kay).

THE BLOOD PHOSPHATASE IN JAUNDICE

Experimentally the blood phosphatase has been increased by ligation of the common bile duct (Bodansky and Jaffe; Armstrong and King; Freeman and Ivy). In 1933, Roberts reported that the blood phosphatase is high in obstructive jaundice. In 21 cases of obstructive jaundice the blood phosphatase ranged from 9 to 23 Roberts units; while in cases of toxic and infective, catarrhal, hemolytic and unclassified types of jaundice the phosphatase was less than 10 units. Roberts, therefore, considered 10 units as the value which may be taken as the dividing line between obstructive and non-obstructive cases of jaundice. Other work (Rothman, Meranze and Meranze) has been published which is in agreement with Roberts. Recently, however, Greene, Shattuck and Kaplowitz have reported that the serum phosphatase is high in acute hepatitis, hepatic cirrhosis and in portal cirrhosis. Cantarow and Nelson in a study of 31 patients with obstructive and 22 patients with hepatocellular jaundice found increased blood phosphatase values in both groups. In general, higher and more often increased blood phosphatase values occur in obstructive than in hepatocellular jaundice, but this distinction has no practical significance from the standpoint of differential diagnosis, since increases are found in both types of cases. The data of the latter two reports thus seem to indicate that the serum phosphatase determination is not of value in the differential diagnosis of obstructive jaundice.

The Phosphatase Unit

Much confusion exists in the literature because of a wide difference in the value of the phosphatase unit of different authors. In terms of normal values the largest unit is about 300 times the smallest unit. Data in terms of one unit cannot be compared satisfactorily with findings expressed in other units because of the different conditions of the laboratory methods used. There is now a tendency toward the adoption of a unit similar to the Bodansky unit based upon a 1-hour incubation of serum or plasma with substrate. The Bodansky unit is defined as "equivalent to the actual or calculated liberation of 1 mg. of phosphorus as the phosphate ion during the first hour of incubation at 37°C. and at pH 8.6, with a substrate containing beta-glycerophosphate, hydrolysis not exceeding 10 per cent of the substrate."

Choice of Method

The phosphatase activity of blood serum or plasma is conveniently and rapidly determined. In my opinion, the Bodansky technic, modified by the use of the Fiske and Subbarow method for the determination of inorganic phosphate, is the most satisfactory procedure for determining serum or plasma phosphatase.

In view of present knowledge, the determination of blood phosphatase is as much indicated in lesions of the bones as the estimation of blood urea in nephritis or of bilirubin in jaundice. There should be a more wide-spread clinical use of this laboratory method.

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ARTIFICIAL FEVER THERAPY OF GONORRHEAL ARTHRITIS*

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For centuries laymen have known and made use of heat for the relief of various human ailments. More than 4,000 years ago the Chinese used heat extensively, and later the Romans and the Greeks established enormous bathing resorts. The baths of Caracalla, for example, consisted of a series of pools in which water was maintained at different temperatures. However, the use of the baths in the treatment of disease was purely empirical, and as a matter of fact in many instances these baths were merely glorified barber shops and houses of assignation.

In Japan, the natural springs of Kutsatu were used from 1700 up to the present in the treatment of syphilis, arthritis and gout. The water from these springs is at a temperature of 100°F. to 160°F., and the bather immerses himself for as long a period as he can stand it, generally 3 to 6 minutes. This is done several times daily for a period of 3 to 5 weeks. However, this again is purely empirical treatment.

True artificial fever therapy really began when Philips in 1884 published his observations on balneotherapy. During a visit to Hot Springs, Arkansas, he noticed that syphilitic patients after a number of treatments left with "faces flushed, eyes brightened, breathing hurriedly and sweating profusely." Inspired by this, Philips experimented on himself and raised his own temperature to 103°F. He concluded his paper with this prophetic remark: "Finally, it is when we are called upon to treat the more chronic forms of syphilitic disease that we are enabled to appreciate the immediate advantage of uniting these powerful constitutional agents (artificial fever and chemotherapy) for good."

The next great work in this field were the history-making researches of Wagner von Jauregg in 1918. The sum and substance of his report was that inoculation with malaria of a patient suffering from dementia paralytica is often followed by improvement or complete remission of symptoms. Since then malarial therapy has been used in numerous conditions with varying results.

This led the way for the use of many types of hetero-proteins, crystalloids, colloids and vaccines for the production of fever. Some of these were fairly satisfactory, others downright dangerous. The most satisfactory still presented these difficulties: (1) Uncertainty of fever production, and (2) complete lack of control of the resultant fever. Therefore, a search was begun for a better method, and recourse was had to physical means.

Among the multitude of physical methods that have been tried are hot baths, diathermy, short waves, ultra-short waves, radiant light, air-conditioned chambers and a thousand and one quack devices. Hot baths are effective for a short time, but after several hours the patient becomes very restless and weakened. Diathermy has its supporters, but this method requires large ventral and dorsal electrodes whose contact, if broken, will cause severe burns. Patients do not like this type of apparatus, since they are confined with but slight motion possible. One of the latest fads is the use of so-called short-wave and ultra-short wave devices. These are merely high-frequency machines. Those with a current frequency of 10,000,000 cycles per second (30-meter wavelength) are called short wave and those with 100,000,000 cycles per second (3-meter wavelength) are ultra short. Some believe that these waves exert an inhibitory or bactericidal effect. Haschė and Leunig dispelled this idea. Krusen states that to date there are very few clinical data to show that short-wave therapy has any great advantage over ordinary diathermy. Radiant-light chambers are fairly satisfactory but take a long time to raise the patient's temperature. One of their chief virtues is their inexpensiveness.

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* Read at the Annual Scientific Assembly of the Society, May 5, 1937.

THE KETTERING HYPERTHERM

I believe that the most satisfactory type of apparatus is the air-conditioned Kettering Hypertherm which has been in use at the Gallinger Municipal Hospital through the courtesy of Mr. Charles F. Kettering and Dr. Walter Simpson. This machine gives the patient comparative freedom of motion and comfort and insures speed of induction and ease of maintenance of fever. There are no mechanical or electrical appliances near the patient, and the apparatus is so arranged that the patient may be withdrawn from it in 5 seconds.

The cabinet resembles somewhat the Drinker Respirator and contains the patient's entire body with the exception of the head. The cabinet is divided into two compartments, the smaller of which contains the mechanical devices and the larger an air mattress on which the patient's body rests. The air is heated by electrodes, humidified by boiling water and projected across the patient's body at the rate of 425 cubic feet per minute by two blowers. The dry heat is accurately regulated by a thermostat and the wet heat by a humidostat. The patient's body is readily accessible to examination by means of large, sliding panels in the wall of the cabinet. An electric fan to play on the patient's face during treatments completes the apparatus.

However, the type of machine used is not nearly as important as the operation of the machine by well-trained and competent personnel. The nurse-technician must possess intelligence, charm and tact. The patient's mental reaction to the procedure is largely dependent upon the nurse's conduct of the treatment.

SELECTION OF THE PATIENT

With an efficient fever-producing apparatus and a competent nurse the next problem is the selection of the patient. Persons over 60 years of age and those with cardiovascular disease or renal pathology are not desirable. Pregnancy and diabetes are not contraindications to this form of therapy. Fortunately, the person suffering from gonorrhea or its complications is generally a young individual in good health otherwise, although possibly cachetic in appearance. The number of cases with definite contraindications is small.

TECHNIC

Before the initial treatment it is wise to order a sedative for the night before, since the patient generally imagines he faces an ordeal. On the morning of the treatment the patient is not given breakfast but is weighed and brought to the fever-therapy room. There his feet are encased in cotton boots and towels are placed over the bony prominences of the body. His temperature, pulse, respiration and blood pressure are taken and he is then put into the chamber which has been heated to 130°F. with a humidity of 75 per cent. The patient's temperature will rise to between 106.6°F. and 107°F. in from an hour to an hour and a half. This is the optimum temperature for the treatment of gonorrheal infections.

As the temperature rises the patient often has a period of mild excitement, particularly between 102°F. and 104°F. A sedative is often necessary. Once this stage is over the patient may sleep, or at least is relaxed and quiet. The skill of the technician is demonstrated by her ability to carry the patient through the treatment with a minimum of sedation. However, when running patients at the high temperature necessary in gonorrhea, morphine is generally necessary to allay the patient's restlessness. I have supplemented this with scopolamine and found it very satisfactory. During the period of induction the rectal temperature and pulse are taken every 15 minutes, and after the temperature reaches 106.6°F. they are taken every 5 minutes.

As the temperature rises the patient perspires freely. It is necessary that the fluid and chlorides thus lost be replaced. This is done by giving the patient an unlimited amount of iced 0.6 per cent saline solution to drink. This generally amounts to 2 to 5 liters. Glucose may be added to the solution to furnish nourishment. If the patient takes enough fluid he will not lose weight during the treatment. Even if weight is lost during an individual treatment the majority of patients gain during the course of a series of treatments because of the tonic effect.

It is necessary for the technician to carefully examine the patient's skin at short intervals to see if an area of erythema is present. If so, the area is covered with ice and the erythema usually subsides. There is a great difference in the ability of individuals' skin to tolerate high temperatures. If the sudoriferous system cannot handle the heat, it is wise to train it by exposure for short periods of time at short intervals. With a preliminary conditioning treatment blistering can be avoided.

As to the length of the treatment in gonorrheal infections, there is great difference of opinion. Some believe, Warren and Carpenter for example, that the treatment should consist of a single prolonged session. They determine the time necessary to kill the particular strain the patient is infected with and then give the patient a treatment of that length of time. On the other hand, Desjardins, Stuhler and Popp favor a series of shorter treatments at 2-day intervals. There is much to be said for both methods, and the individual patient's condition and personnel limitations must dictate the choice. After the temperature is elevated restlessness can be controlled indefinitely by the judicious use of sedatives, and it is only a very occasional patient who is exhausted by the long treatment. Unfortunately, because of personnel problems it is difficult in most institutions to give treatments of over 8 hours of high fever. At Gallinger Municipal Hospital, due to the small number of nurses in proportion to the large patient turnover, it is absolutely impossible.

COMPLICATIONS

The most frequent complication is burns. As stated before, with good management these can be kept to a very small percentage. In gonococcal treatments there has never been a severe burn at Gallinger Municipal Hospital. A number of patients develop herpes following the initial treatment. These are blemishing but of course disappear in a short time.

The next most frequent complication is tetany (both chloride- and calcium-deficiency forms). If saline is given freely this is not frequently seen. If it does occur, it can be easily relieved by the intravenous administration of saline solution and calcium.

Cerebral edema occasionally occurs in elderly patients, particularly in those patients who are very deteriorated paretics. A patient of this type is of course removed from the cabinet and given 50 per cent glucose solution intravenously and carbon dioxide and oxygen inhalation therapy if necessary.

I cannot emphasize too much the fact that in competent hands this is a safe form of therapy. At Dayton, Ohio, in 4 years of artificial fever work, not one patient has died despite the fact that it was there that the pioneer work was done with an air-conditioned cabinet. In 4,809 cases the mortality rate was 0.6 per cent. On the other hand, this work if done by the incompetent or the actually unscrupulous is fraught with the greatest dangers. This is not an office procedure but one that is solely adapted for hospital use.

DESCRIPTION OF A TREATMENT

At the institutions where the Kettering Hypertherm is being used all the physicians and nurses doing this work have had at least one treatment themselves. It is not at all terrifying if the subject has been carefully prepared psychologically. On first entering the cabinet there is a delightful sensation of warmth of the body, but the face feels cool due to the electric fan. In 15 minutes or so, one notices a great deal of perspiration, then the respiration becomes accelerated and the heart pounds slightly at an increased rate. This is the point where one welcomes the nurse's reassurance. A little later one feels very warm, but this is compensated for by drinking the iced saline solution and by the nurse wiping the face, head and neck with ice water. At this time one feels completely relaxed and may then fall into a sound sleep.

Waking, one may be restless, since it is difficult for most people to stay still several hours in one position even though one may turn in any direction desired. A hypodermic then recaptures the previous state. At the conclusion of the treatment, after removal from the cabinet the main sensation is one of great weakness. After lying in the air the strength gradually returns, and in an hour the temperature has returned to normal. After a 5-hour treatment of 105°F. to 106°F. the average person can get up and go home unaided.

To speak briefly of the physiological changes that occur during a moderate treatment (105°F. to 106°F. for 5 hours), the pulse rate increases rapidly as the temperature rises. It may reach 160 and become stabilized or, on the other hand, perhaps only 120. The average is about 130. A rate that is normal in one individual may be dangerous in another. Only experience gives this judgment. The systolic blood pressure rises during the first hour of treatment, possibly 10 to 20 mm. of mercury, then it gradually drops from 10 to 40 mm. below the original figure. The diastolic pressure continually falls, perhaps 10 to 30 mm. in all. The respiration increases sharply at first to perhaps 40 per minute and later becomes stabilized at about 28. The basal metabolic rate increases to plus 35 per cent. The electrocardiogram shows an inversion of the T wave, which returns to normal at the conclusion of the treatment. There is a leukocytosis, predominately polymorphonuclear-neutrophilic in character with a relative lymphopenia. The leukocyte count ranges from 20,000 to 60,000. As can be seen then, there is a general stimulation of bodily activities which is demonstrated in the tonic effect a series of treatments has on an individual patient.

RESULTS IN 43 CASES OF GONORRHEAL ARTHRITIS

Among the diseases that have been treated with favorable results at Gallinger Municipal Hospital are syphilis (primary, secondary and tertiary), chorea, intractable asthma, nonspecific arthritis, peripheral vascular disease, toxic neuritis, iritis, and all forms of gonococcal infection. At this time I am reporting 43 cases of gonorrheal arthritis treated in the Kettering Hypertherm in the last year and a half at that hospital. These cases were treated in order of admission to the hospital and were not selected in any sense of the word except cases were ruled out that presented contraindications to fever therapy. Where there was a choice of cases, the one chosen for treatment was always the one which had received other forms of therapy without result.

The cases ranged from 12 to 47 years of age, the average age being 26 years. Twenty-seven of the patients were white and 16 colored. There were 9 females.

The greatest length of time a patient had suffered from gonorrheal infection was 8 years, although 1 patient said he had had it "off and on" for 20 years. The shortest period was 3 weeks, the average being 14 months.

The duration of the arthritis ranged from 1 week to 5 years. Twenty-four of the patients had had arthritis 2 months or less.

Nineteen patients had single-joint involvement, the rest having multiple-joint involvement. For simplification of description, the patients were arbitrarily divided into four groups so far as joint pathology was concerned. Those in group 1 had had slight joint involvement, while those in 4 were confined to bed with marked pain, swelling, ankylosis and perhaps erosion of bone as demonstrated in X-ray films. Thirteen, or almost one third of the group, fell into group 4 classification, while only 6 patients composed group 1.

The percentage of improvement of the group ranged from 0 to 100 per cent. The 1 patient with no improvement had a negative smear before and after the treatment. It seems likely, in view of our results, that this patient probably had a nonspecific urethritis with a coincidental rheumatoid arthritis. The average improvement of the entire group was 90.2 per cent. Of those in group 4 the average improvement was 88 per cent. The average improvement, therefore, in the other three groups was 93 per cent.

Of the 43 cases, 14 had received typhoid vaccine intravenously, 7 Corbus-Ferry filtrate, 1 protein-shock therapy, 8 only local treatment and 14 no treatment. Only 2 patients had negative smears when examined by us before treatment. At the conclusion of fever therapy all patients with the exception of 1 had negative smears. It is believed that the positive smear occurred in this case because of the lack of a prolonged treatment.

Of these patients 7 were classified as being in a poor condition. In other words, due to toxemia they were absolutely confined to bed with low blood pressure, rapid pulse and a "washed out" appearance. Nine patients were in only fair condition. At the conclusion of treatment all of the patients with the exception of 1 were ambulatory, nearly all had gained weight, the pulse rate had decreased, blood pressure had risen, and all looked like new people.

So far as the number of treatments is concerned, the minimum was 1, the maximum 14 and the average 4.2. The hours of fever between 106.6°F. and 107°F. ranged from 6 to 61. The average number of hours was 24. With more experience the number of treatments and the number of hours of high fever have been cut down.

Thirty-three or three fourths of the patients took the treatment uneventfully. One patient became exhausted in his second treatment and was removed from the cabinet, and his treatment was resumed at a later date. One patient developed tetany, and the treatment was resumed after administration of calcium. One patient became violent in his third treatment due to insufficient sedation, and the treatment had to be discontinued.

One patient developed jaundice after his first treatment with a direct van den Bergh reaction with serum bilirubin of 15 mg. per cent. He recovered in 10 days and fever therapy was resumed. One patient developed anesthesia of a small area of both legs which regained sensation in a week. One patient had respiratory collapse during the second treatment, and his treatments were then discontinued. One patient after 6 treatments showed albumin and red blood cells in his urine, and his treatments were discontinued. One patient developed a slight peripheral neuritis which may have been due to his having been on a restricted protein diet for a long period of time prior to treatment.

Fourteen of these patients required physiotherapy at the conclusion of fever therapy and 2 required forcements brisé which were followed immediately by a fever treatment.

All of these patients were improved by the supplemented treatment.

CONCLUSIONS

1. Artificial fever therapy with cautious use is a safe form of therapy.
2. Forty-three cases of gonorrheal arthritis, the majority of which received other forms of treatment without benefit, were treated with artificial fever therapy. The average improvement of the entire group was 90.2 per cent.
3. Of these cases 41 had positive smears from the genito-urinary tract before treatment, and all but 1 were negative at the conclusion of treatment.
4. Artificial fever therapy appears to be the procedure of choice in the treatment of gonorrheal arthritis.

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NEURODERMATOSES*

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The association of various dermatoses with functional nervous disease may be divided roughly into two groups: (1) Those diseases that are clearly psychoneuroses; (2) those in which there is a clinical assumption of nervousness as an etiological factor.

In the first group may be placed trichotillomania and the neurotic excoriation group.

Trichotillomania is the deliberate pulling out of hair, usually in the scalp. It is seen most often in mental institutions, but may be encountered in outside practice. The patients pull the hair out in patches, sometimes all over the scalp and at others in one area only. In the milder cases the disease is probably a form of compulsion neurosis, usually encountered in patients seeking sympathy. Another form of the disease is sometimes seen in orphanages. Here one of the youngsters develops either alopecia areata or tinea capitis, and other inmates in imitation of the afflicted patient pull out the hairs in crops. This is probably the explanation of reported epidemics of alopecia areata in institutions. The appearance of the scalp in these cases is an irregular alopecia, with areas of baldness, not perfectly round, where the hair has been recently pulled, and scattered areas of hair of irregular length where regrowth in various states has occurred, and with no local or constitutional disease to account for the trouble. There are several types of neurotic excoriations.

1. *Dermatitis artefacta.* These are excoriations or chemical or mechanical ulcers on the skin deliberately produced by malingerers who always deny their part in the production of the lesions. Their type of dermatitis can be spotted almost at once because the artificially produced lesions always appear in bizarre forms that can never occur in natural disease, with angles and lines that do not simulate the curved borders always seen in normal diseased lesions, and always in areas easily accessible to the patient's hands. This type of eruption is usually found in compensation cases, in those seeking legal easy money, and in those who crave sympathy and avoid working by the production of disease. They deserve no sympathy and should be handled "without gloves."

2. *The tic or "pickers disease" group.* These patients habitually pick at their skins, usually at some slight defect in the skin such as comedone or keratotic plug, but sometimes at perfectly normal skin. The lesions are seen most often on the face and scalp, and are simple excoriations. The patients are perfectly conscious of what they are doing, make no effort at concealment, and simply state that they are unable to control the habit. The commonest basic skin disease in these patients is an acne, and often the correction of this and the use of repeated suggestion and encouragement will overcome the disease. Recurrence, however, is common.

3. *The compulsion neurosis group, or acarophobia.* These patients also do not deny that the excoriations are self-induced. They are convinced, however, that there is a parasite in their skin and they make heroic efforts to remove the supposed parasite, even to the extent of causing ulceration, either with the nails, or with an instrument. They will always present small pieces of epidermis or crust or cotton lint as proof that there is a parasite. The delusion is usually firmly fixed and no amount of persuasion or assurance will change the patient's attitude. Such patients are commonly seen in mental institutions, but in ordinary private practice they seem otherwise normal and are able to carry on their regular work but cannot overcome their supposed infection.

Two other conditions which may be related to milder forms of psychoneurosis are essential pruritus, and hyperidrosis.

Generalized pruritus for which no physical cause, such as scabies and pediculosis, carcinoma, diabetes, or allergy can be found, is often caused by various types of mental strain. The same may be said of localized pruritus of various types, especially pruritus ani and pruritus of the genitalia. Pruritus ani is often due to physical causes, such as fissure, hemorrhoids and local infection, particularly mycotic infection. But there remains a large group of cases in which no local pathology can be found, which are often resistant to treatment, and which have a marked tendency to recurrence. For these cases there seems no other explanation than that the itching is the expression of a neurosis, and one usually notes that these patients are the repressed or highly strung type of individual. The same condition holds true of pruritus vulvae and pruritus scroti. If the urine is sugar-free and there is no vaginal discharge or local mycotic infection, the etiology is most likely to be a neurosis, and in these cases often a sex neurosis.

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* Read at the Annual Scientific Assembly of the Society, May 5, 1937.

Hyperidrosis, especially of the palms and soles, and occasionally hyperidrosis and bromidrosis in the axillae and groins, are found in the highly strung and nervous type of patient. Among veterans the symptom of hyperidrosis of the palms and soles was found almost exclusively in those carrying a basic diagnosis of psychoneurosis. This experience in the hospital has been borne out in private practice, and I believe this symptom is almost always based on a nervous disturbance.

So far the relation of conditions discussed to functional nervous disease is fairly clear. There is a whole host of other skin diseases in which "nervousness" is mentioned as a factor. Several types of eczema, lichen planus, acute outbreaks of psoriasis, alopecia areata, dermatitis herpetiformis, urticaria and angioneurotic edema may be mentioned as examples. Personally, when, in the study of these cases I find myself falling back on the explanation, "nerves," I feel that I am either too lazy to hunt for the real cause, or that in the present state of our knowledge the etiology cannot be determined. It is like the term "idiopathic" that was so popular when I was a student—it covers a vast amount of ignorance. That mental tensions, worry, overwork, etc., may play a part in all of these conditions cannot be denied. There can, I think, be hardly any disease process in which the mental state does not play some part. But "nerves" as the ordinary practitioner usually understands it, may be anything from the fact that the breakfast egg was not properly cooked to too much or too little sex life. Understood so, there is probably no person in our highly developed civilization who is not so afflicted, and we are leaning on a weak pillar when we place all the blame for any of these disease processes on this etiologic factor. Nevertheless, with this admission of weakness, there are certain cases of chronic urticaria and chronic eczema of the lichenified type which do seem to be primarily due to mental strain of one type or another. Personally, I do not believe that dermatitis herpetiformis, psoriasis, or lichen planus are in any way due to nervous disease.

Special note should be made of neurodermatitis. This term was originally introduced into American usage by Fred Wise, of New York. I was in the clinic when he started work on this group, and by the term he originally meant that group of cases which had previously been described as lichen chronicus simplex, a form of eczema. The reason for the new term was that at that time it was felt that the patient had a local pruritus of nervous origin, and that scratching this produced the eczema. Whether or not this is true, the term has been applied by different men to cover not only lichen chronicus simplex, but flexural eczema, and generalized lichenified eczema. The latter are undoubtedly atrophic forms of allergy, and as even the etiology of the first group is in doubt it would probably be best to drop the term altogether, as its use at present leads only to confusion.

Conclusions

1. Trichotillomania, dermatitis artefacta, "picker's disease," and acarophobia are definite cutaneous psychoses.

2. Hyperidrosis and certain forms of pruritus are definitely associated with milder grades of psychoneurosis.

3. There is probably a strong psychotic element in certain cases of chronic urticaria and certain types of chronic eczema, especially lichenified eczema.

ENDOMETRIOSIS*

Report of Two Cases

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The clinical entity commonly spoken of as endometriosis has been recognized since the beginning of pelvic surgery. Cattell and Swinton state that von Rokitansky in 1860 was the first to describe adenomyoma as a pathological entity; von Recklinghausen in 1893, the first to blame the occurrence of these tumors on cell rests in the wolffian ducts; and Cullen in 1896, the first to mention adenomyoma of the round ligament.

In 1899 Russell (according to Davis and to Sampson) described for the first time endometrial tissue in the ovary, and in 1905 Ludwig Pick (according to Sampson), reported 4 cases called adenoma endometrioides ovarii, which was the first description of the typical chocolate cyst of the ovary. Up to 1921 when Sampson made his report covering 23 cases of adenomyoma, or endometriosis, less than 20 cases had been reported in the literature. His study focused the attention of the profession upon the significance and appreciation of this condition as a clinical entity worthy of careful study. Like so many intriguing problems in which the solution is not clear cut, many theories have been advanced to explain this condition. These theories really parallel the appearance and description of the growths as first described by the original writers. Von Recklinghausen (according to Lockyer) tried to explain such tumors as derivatives of the wolffian system, and Russell (according to Attygalle and Misso, and to Davis) considered them to be of Mullerian origin. Cullen in 1896 advanced the theory of diverticular outgrowths from uterine mucosa into the myometrium. This is one of the oldest theories and still seems valid for the diffuse type of uterine growth. When the growths were found in less easily explained locations, such as intestines and umbilicus, the serosal metaplasia theory as advanced by Meyer, Nichalson, and Ivanoff appeared (Davis; Lockyer; and Sampson). This theory purports that when any epithelial surface is submitted to the influence of chronic irritation, the cells will so alter their character as to become either cylindrical or cuboidal and will proliferate and begin to invade the adjacent tissue. Thus the peritoneal mesothelium is a source of endometrial growths. This remained the theory of choice until Sampson's idea that the process resulted from living menstrual grafts, or of misplaced tubal or uterine endometrium appeared. In 1924 Halban advanced the lymphatic theory and was supported in his views by Schiller and Litzenfrey (Attygalle and Misso). The latest suggestion, the hormone idea of cellular metaplasia caused by glandular dysfunction, as suggested by Allen, is worthy of consideration. In support of his theory Allen calls attention to certain outstanding features such as the high incidence of menstrual irregularities (glandular imbalance); associated benign uterine tumors; marked prevalence of relative sterility (given as 60 per cent in Allen's series); and the wide distribution of the lesions in endometriosis. He believes that such facts necessitate the acceptance of the theory of combined mechanical dissemination as suggested by Sampson, or the theory that isolated islands of normal cells may undergo a change in cell type into endometrial-like tissue under the proper hormonal stimulation. Witherspoon supports the hormonal stimulation idea by finding the estrogenic principle the common etiological factor in endometrial hyperplasia, uterine fibroids and endometriomas. He presents clinical and pathological data to support his views.

Weller, writing on the ectopic decidual reaction and its significance in endometriosis, calls attention to a nodular or plaque-like decidual reaction of the subserosa which not infrequently makes possible the differential diagnosis of pregnancy from appendicitis even though the pregnancy is unknown to the pathologist. Such ectopic decidual reactions have been found upon the ovary, oviduct, broad ligament, anterior rectal wall, small intestines where adherent in the pelvis, and the omentum when adherent to an oviduct in which there was an ectopic pregnancy. In contrast, Schiller has shown the development of decidual formation in similar locations in the apparent absence of pregnancy. Weller further points out that regional distribution of endometriosis coincides with that of the ectopic decidual reaction. In view of these facts it is reasonable to assume that the mesothelial cells likewise possess latent potentialities and under hormonal stimulation produce the epithelial elements in endometriosis. Regardless of the theory accepted to explain their origin, these growths wherever found behave as miniature uteri with the same functional and cyclical changes as the normal endometrium.

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* Read before the Washington Gynecological Society, December 4, 1936.

The age of occurrence parallels the age of menstruation. Meigs in 1930 reported finding it in a patient 23 years of age, and Allen in his report stated that the earliest case was in a patient 17 years of age. In his series of 112 cases he found 24 patients between 20 and 30 years of age; 39 patients between 31 and 40 years of age; 42 patients between 41 and 51 years of age; 5 patients between 52 and 55 years of age; and 2 patients older than 55 years, the oldest being 67.

The ovary is the most common site, the growth being more often on the posterior surface. Keene and Kimbrough in 119 cases gave the frequency of location as follows: ovary 110, rectovaginal septum 6, umbilicus 2, and laparotomy scar 1. Allen in his series of 112 cases found the lesion occurring 177 times with the distribution as follows: ovaries 60, uterus 53, peritoneum 16, rectovaginal septum 37, bowel 4, abdominal 3, bladder 3, appendix 1. Figures for the number of cases reported in laparotomy scars are not so readily available. Heaney in 1925 found that 29 growths of this type, subsequent to abdominal operations, had been reported: 14 followed ventral fixation, 2 hysterectomy, 3 pelvic operations, 2 appendectomy, 1 oöphorectomy, and 7 operations in which the pregnant uterus had been opened. To these 7 cases Heaney added 2 cesarean section cases of his own, and Danforth added an additional case. Similar cases have been reported by Meigs, Allen, Keene, Crowley and others.

The clinical picture of pelvic endometriosis is not always clear, and the diagnosis is seldom made prior to operation. The prominent symptoms are menorrhagia, backache, dysmenorrhea and lower abdominal pain, and bladder and rectal pain with menstruation. When the growths are located in laparotomy scars they usually produce some swelling with pain beginning about 10 days before menstruation and lasting throughout to several days after the period. The presence of a menstruating sinus associated with the above symptoms confirms the diagnosis.

Conservatism is now the general rule in the treatment of this condition, and whenever possible some ovarian tissue should be left even though a second operation may be necessary later. Castration either by operation or X-ray is reserved for those patients at or near the menopause, for recurrent symptoms demanding relief, and for those who present lesions involving important structures or too extensive to be resectible.

I report here 2 cases of endometrial growths, 1 removed from an abdominal scar following a previous bilateral salpingectomy and ventral suspension, and the other occurring in the pelvis following a panhysterectomy.

REPORT OF CASES

Case 1: Mrs. O. S., white, aged 30 years, was first seen on May 11, 1936, for the following complaints: backache, severe menstrual discomfort, bladder frequency, low abdominal discomfort, and tender painful anterior abdominal wall. She stated that her present illness really began 9 years before, following an operation for a tubal pregnancy. At this operation both tubes and the appendix were removed, the uterus suspended to the anterior abdominal wall, and a drain inserted and brought out through the lower pole of the incision. Her convalescence after this was quite long, and on reappearance of menstruation her complaints began. For 2 years she menstruated regularly through the sinus tract where the drain had been, and when the opening gradually closed she began having severe abdominal discomfort in the region of the scar. This discomfort would begin about 10 days before each period and gradually subside in about the same time after the flow. During this time the scar and the abdominal wall became so painful and tender that the patient began wearing a reinforced corset for her protection. In fact, she stated that she was always in mortal fear of a blow or injury to her stomach. With the development of the abdominal discomfort severe menstrual cramps with radiating pains to both legs and back appeared. These symptoms finally became so severe that the patient was forced to seek medical aid even though fearing a second operation.

She had had most of the usual childhood diseases. Menstrual periods began at 11 years of age, lasted 5 days and were regular every 28 days with slight cramps. She had had the abdominal operation which has already been described. Four years before she had been treated for an irritating vaginal discharge with good recovery. The family history was of no relative importance.

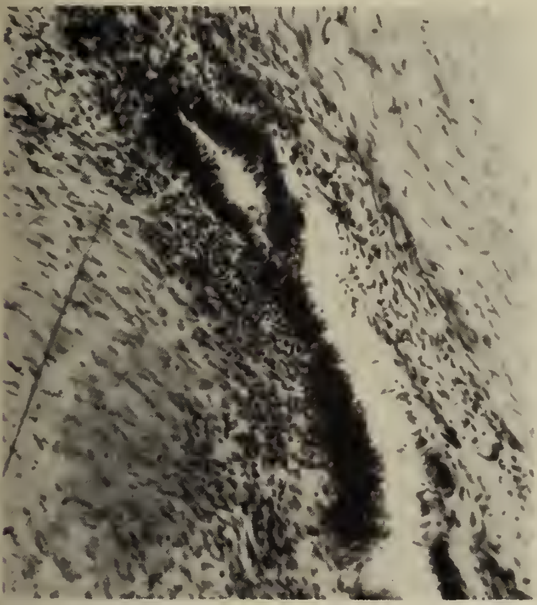

Fig. 1. Case 1. Section of Tissue Removed from Anterior Abdominal Wall Showing Uterine Gland Lined with Cuboidal or Columnar Epithelium

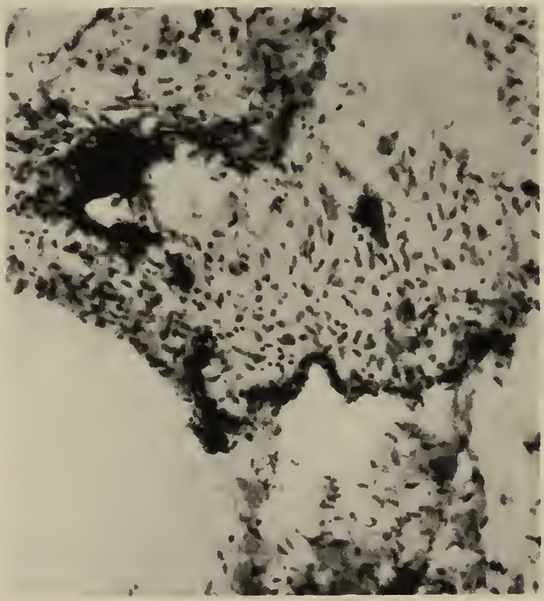

Fig. 2. Case 2. Section of Wall of Cyst Showing Portion of Gland Space Lined with Columnar Epithelium

Physical examination revealed a well-developed, well-nourished and well-cared-for young white woman. The findings were essentially negative except for the abdominal examination which revealed a very wide low mid-line scar which contained a definite irregular mass extending about half-way from the symphysis pubis to the umbilicus and to either side of the mid-line a distance of 1½ inches. This entire area was fixed and very tender, and the skin here presented evidence of the old sinus tract. The combined abdomino-vaginal examination revealed that the uterus was firmly attached to the area above described. The adnexae were not made out. The cervix was clean and there was no vaginal discharge.

At operation on May 15, 1936, the abdomen was opened through the old scar and the area at the lower pole dissected free and removed. This area extended through the thickness of the abdominal wall and involved some of the rectus muscle on both sides of the mid-line, but it did not extend through the peritoneum. It was composed of scar tissue, muscle, and many small cysts filled with old, "tarry" blood. The uterus was found firmly attached to the anterior abdominal wall by a well organized band of scar tissue. This was separated and the point of attachment to the fundus closed. Both tubes had been removed and the round ligaments had been brought forward and anchored to the anterior surface of the uterus. The left ovary was enlarged and contained many follicular cysts. It was removed. There were also many well organized adhesions between the small intestines and the anterior parietal peritoneum which made the entry very trying. The abdomen was closed in layers, convalescence was uneventful and at present, 5 months later, the patient has returned to work minus her abdominal pain as well as her corset.

Paraffin sections of the mass removed from the abdominal wall showed fibrous or fibromyomatous tissue with blood vessels, round-cell infiltration and a number of gland spaces, occasionally dilated to form small cystic spaces. These were lined by cuboidal or columnar cells and had the appearance of the epithelial structures of uterine mucous membrane (Fig. 1). The process was evidently endometriosis.

Case 2: Mrs. M. F., a white woman, aged 30 years, first examined on February 1, 1936. Her present illness began 3 weeks before with gradual and painful enlargement of the lower abdomen, painful defecation, and urinary frequency. She had had the usual childhood diseases. In 1927 she had had a full-term pregnancy with a normal spontaneous delivery. In 1932 an appendectomy and uterine suspension were performed. During the following year a hemorrhoidectomy, excision of anal fissure, and a cervical cauterization were done.

Her tonsils had been removed. She also stated that she had had syphilis and had been given several courses of treatment for this disease. In 1934 a panhysterectomy and bilateral salpingectomy were performed for chronic pelvic inflammatory disease. No mention was made on the operative record of the disposition of the ovaries at this time, although the patient was told that one was removed. Following this last operation the patient remained fairly well with the exception of occasional attacks of pain on defecation until the onset of her present illness. Her family history was essentially negative.

Physical examination revealed a well-developed, well-nourished, young white woman not acutely ill. Examination of the abdomen revealed a definitely outlined mass of the consistency of a distended bladder arising from behind the symphysis pubis and reaching mid-way to the umbilicus. Abdomino-vaginal examination after catheterization revealed that the cervix had been removed and that the entire pelvic cavity was filled with a soft cystic tumor almost the size of a 5-month's pregnancy. The diagnosis of ovarian cyst was made and an operation advised.

The abdomen was opened through the old mid-line scar. A large cystic tumor was found arising from a broad base in the pelvis, completely closing this cavity to exploration. The wall of the cyst, which was closely adherent to small intestines above and the bladder anteriorly, was thick, edematous, and very friable. Manipulation caused accidental rupture of the cyst and revealed it to be multilocular, with many small pockets filled with old "tarry" blood. No ovarian tissue was identified and when the contents of the cyst were aspirated many small "raspberry-like" nodules were found scattered over the structures in the culdesac. The general impression was that the point of origin was over the previous vaginal closure beneath the peritoneal reflection which had been dissected upwards to form the wall of the cyst.

The diagnosis made at the operating table was that of extensive pelvic endometriosis. A portion of the wall of the cyst was removed for examination. The patient made an uneventful convalescence, and when up and around she was sent to the X-ray department where she was given 4 treatments of 1,000 Roentgen units to each of 4 areas, namely, anterior pelvis, posterior pelvis, lateral right pelvis, and lateral left pelvis, making a total of 4,000 Roentgen units. The last examination of this patient was made on August 18, 1936, 6 months after the operation, when she was found to be completely recovered and back to work.

Histological examination of the tumor wall revealed rather loose, vascular, and edematous connective tissue, with one area showing gland space lined with columnar or cuboidal epithelium (Fig. 2). The diagnosis was endometriosis.

The dense peritoneal adhesions in this case, the friable, edematous cyst wall, and the multilocular character of the cyst with its "tarry" blood contents are characteristic features of endometrial growths. The X-ray therapy was used to destroy any remaining ovarian tissue and thus to prevent any possible recurrence of the condition.

SUMMARY

A brief consideration of the subject of endometriosis, together with a report of 2 cases, 1 removed from an abdominal scar following a previous bilateral salpingectomy and ventral suspension, the other occurring in the pelvis subsequent to panhysterectomy and excised and followed by irradiation has been presented.

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ASTHMA FOLLOWING PROLONGED EXPOSURE TO SULPHUR DIOXIDE*

Report of a Case

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Leakage of sulphur dioxide from electric refrigerators represents an industrial hazard which is increasing in frequency. Refrigerator repairmen are particularly exposed. The following case is reported to show that the gas may have unfortunate effects upon a person whose respiratory tract is especially vulnerable.

REPORT OF CASE

W. N., a 25-year-old white man, began work August 15, 1936, as a refrigerator repairman. He worked all day with another man in a room about 10 feet long by 8 feet wide. The one small window in the room was kept closed, and the exhaust fan to the outside could be run only one half hour per day, when the refrigerators were not being taken apart. Although the patient had been perfectly well when he began work, he noticed a slight cough during working hours from the first day of employment. This was particularly marked on the days when refrigerators were taken apart and a large amount of sulphur dioxide allowed to escape. On the days when the cough was at its worst, the patient also had cough after he left work. After about 4 days of work, the cough became productive of yellowish sputum, which gradually became more abundant. Dyspnea on exertion and generalized weakness also became prominent symptoms. On September 26, 1936, the patient felt so weak and dyspneic that he had to leave work early, and from that time on he was unable to work. That night he could not lie down because of coughing and dyspnea. For the next 6 weeks he slept sitting up, leaning his elbows upon a table.

The other repairman, who worked in the same room, had a cough on contact with the sulphur dioxide fumes, but he did not develop any other symptoms. His cough did not continue after he left work.

The patient had had none of the major infectious diseases. One winter, when he was 8 years of age, he had slight asthma on a few occasions. This condition stopped without any treatment, and he had had no recurrence for the intervening 17 years. He had had no other allergic diseases.

The family history revealed that his mother had previously suffered from asthma.

On physical examination the patient coughed at frequent intervals, and upon attempting to lie down he had a paroxysm of coughing with the expectoration of a moderate amount of yellow, purulent sputum. Nothing of note was found upon examination except a moderate number of sibilant and mucous râles through both sides of the chest.

The urine showed a very faint trace of albumin and a rare white blood cell and red blood cell. The hemoglobin was 89 per cent (Sahli), the red blood cells numbered 4,560,000 per cubic millimeter, and the white blood cells, 14,600, with 78 per cent polymorphonuclear neutrophiles, 15 per cent lymphocytes, and 7 per cent eosinophiles. The sputum contained many pus cells and a moderate number of eosinophiles. No tubercle bacilli were found. Roentgenograms of the chest showed a moderate increase in bronchial fibrosis, radiating from the hilar regions to both apices and bases. Intradermal tests with the common inhalant and food allergens revealed no sensitivity considered to be significant, except a marked (3 plus) reaction to house dust.

The patient was given codeine for the cough and a sedative for sleep as a temporary measure. These enabled him to sleep for several hours, but still only in a sitting position. Beginning November 12, 1936, the patient was injected subcutaneously with increasing doses of 1:10 dilution of the house dust extract to which he had shown sensitivity. At the same time all possible sources of dust were removed from his environment. Improvement began coincident with this therapy. In 1 week he was able to sleep without pillows and 2 weeks after injections were begun he coughed only occasionally and slept the night through in a horizontal position. Examination of the chest at this time showed only a few mucous râles at the extreme left base posteriorly. Improvement has continued since then, but more gradually. At the present time, 4 months after the inception of treatment, the patient is still receiving weekly injections of full strength house-dust extract. Although nothing abnormal can be heard in the chest, he still coughs infrequently and expectorates a small amount of yellow, purulent sputum. He becomes dyspneic after moderate exertion, and consequently is unable as yet to return to his usual occupation.

COMMENT

The inhalation of sulphur dioxide has two possible medical implications: (1) The immediate toxic effect, and (2) the delayed or chronic effect. Since the gas changes into sulphurous acid on contact with water, it is quite irritating to the respiratory passages, its acrid fumes inciting the coughing which is so familiar to those who have performed blood nonprotein nitrogen tests. Inhalation of concentrations of 0.001 per cent by volume cause extreme discomfort, while 0.1 per cent causes death by paralysis of the respiratory center.) Actually these concentrations are practically never found in industry, or, if they are, the odor and cough give sufficient warning to allow egress to the open air in time.

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* Read before the Section on Internal Medicine of the Society, November 27, 1936.

On the other hand, refrigerator repairmen are continually exposed to the inhalation of sulphur dioxide throughout each working day over many years. It is important to determine whether any permanent disease results. Workers in the Medical Research Division of the Chemical Warfare Service, United States Army, according to Vedder, exposed mice, rats, guinea-pigs and rabbits to low but noticeable concentrations of sulphur dioxide, under carefully controlled conditions of temperature and moisture, for periods of 6 months. These animals lived normally, and multiplied and raised their young, although the concentrations used destroyed growing plants. The investigators were unable to demonstrate any pathological changes in the tissues of the exposed animals.

Kehoe and his associates, working at a plant where electric refrigerators are manufactured, compared 100 persons exposed continuously to sulphur dioxide over varying periods of time up to 12 years, with a group working in the same factory who had never been exposed to the gas. The groups were similar in age, sex and length of service. In the exposed group there were found: (1) A higher percentage of cases of chronic pharyngitis and tonsillitis, (2) alteration in the senses of smell and taste, (3) dyspnea on exertion, and (4) increase in fatigability. On the other hand, roentgenograms showed no greater incidence of lung changes in the exposed than in the control group. The authors concluded that, while temporary changes in the membranes of the air passages resulted from continued exposure to sulphur dioxide, no permanent changes took place.

In the present case, the patient had several indications of the allergic state: (1) The history of asthma in his mother, (2) the occurrence of asthma in the patient as a child, (3) the high percentage of eosinophiles in the blood and sputum, and (4) improvement occurring at the same time as hyposensitization. It may be postulated that the patient had an allergic constitution with no clinical symptoms for the previous 17 years, and that the inhalation of the sulphur dioxide acted as an irritant to the respiratory mucosa, permitting the dust allergen to excite asthma as a symptom-complex. The pathologic state of the bronchial mucous membrane in asthma offered a favorable medium for the growth of bacteria, and this, together with the continued irritating effect of the sulphur dioxide in lowering the resistance of the bronchial tissues, accounts for the development of the asthmatic bronchitis.

SUMMARY

1. A case is reported in which symptoms of asthma developed in a person with an allergic constitution after repeated and prolonged exposures to inhalation of sulphur dioxide.

2. According to the best evidence available, the inhalation of sulphur dioxide over a long period of time causes no permanent damage to experimental animals or normal human beings.

3. Persons with an allergic history or background should not be exposed to sulphur dioxide over any considerable period of time.

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PREPAYMENT OR POSTPAYMENT?

Many members of the Society have manifested considerable concern over the organization of the Group Health Association, Inc., which proposes to provide complete medical care, including hospitalization, for all employees of HOLC and, if the board of trustees desires, all government employees. They fear that this organization is the first unit, an experimental one perhaps, in a plan to provide medical care for all government employees. Such a program on superficial reflection would appear to affect seriously the private practice of medicine in the District of Columbia and to a less extent throughout the United States. A masterful article on the subject of Group Health Association, Inc., appeared in the October 2 issue of the Journal of the American Medical Association. This article exposes the shortcomings of such an organization.

Although the Society on October 7 formally condemned the principles of Group Health Association, Inc., and voted in effect to expell all members who became associated with it, some agitation has developed in the Society for the formation of a similar competitive organization for members of the Society.

Prepayment plans for medical care have been condemned by the American Medical Association. In such plans there are not only too many possibilities for the exploitation of the services of physicians, but there are also possibilities for the lowering of the standard of medical care. Both the medical profession and the public would undoubtedly suffer. The agitation for such plans, which would bring about the socialization of medicine, is fostered by well-intentioned sociologists and crafty politicians.

The development of a prepayment plan for medical care to involve the services of a society of some 800 physicians would be complicated and expensive. It is hardly likely that a majority of members would be willing to cooperate in such a plan even if a change of attitude toward such plans should develop.

To begin with, there is no necessity for such a plan for medical care in the District of Columbia any more than there is the necessity for such a plan for furnishing a house or buying groceries. The only difference is that medical needs are largely unpredictable and may unexpectedly call for relatively large expenditures. It is just as simple to defray expenses incurred by sickness on the instalment plan as it is to buy furniture in that way. The Society has already established the machinery for such a method of instalment buying of medical care under the auspices of the Medical-Dental Service Bureau, Inc., which is a unit of the Health Security Administration of the District of Columbia with offices at Eighth and Eye Streets, N.W. Many patients in the lower income brackets have availed themselves of the services of this Bureau during the past three years. Not only does the Bureau act as financial secretary for these people but it helps them to budget their incomes and it makes it possible for them to defray their medical debts within a reasonable length of time according to their ability to pay. Many times this is possible only by a scaling down of fees by physicians. In all such instances in the past physicians involved have unhesitatingly agreed to reduce their fees. This method of medical financing does not in any way alter the time-honored relationship of patient and physician.

The only difficulty in developing this plan to its fullest has been a reticence on the part of many physicians to allow their patients to use it. Furthermore, there has not been sufficient publicity to make the public conscious of its existence and its advantages. The plan is simple, relatively economical, and not tainted with the weaknesses of socialized medicine. The reticence of physicians to utilize the Bureau, innocuous as it is, is an indication of a greater hesitancy that would appear if a complicated, expensive and restrictive prepayment plan were proposed.

It is improbable that the Group Health Association, Inc., will meet with much enthusiasm from the public. The standard of living in America is so high, the privilege of selecting his own physician is so firmly implanted in the mind of the average American citizen, and his distrust for institutional and mass service so great, that many of those eligible to join such an association will fail to join it or will cease to use it. Nevertheless it behooves the physicians of Washington to demonstrate their desire to make adequate medical care readily and freely available to all. This can be done by means of whole-hearted coöperation with the Medical-Dental Service Bureau.

Certainly, the Medical Society of the District of Columbia should not allow itself to be stampeded into precipitate and regrettable action.

COMING MEETINGS

Wednesday, November 3: Stated Meeting of the Society. Election of members; reports of officers and committees, etc.

Wednesday, November 10:

1. "Mortality in Acute Empyema Thoracis." Illustrated. J. Lloyd Collins, M.D.
2. "Serum, Antitoxin, Vaccines, and Drugs in Prevention and Treatment of Meningococcus Meningitis." Sara E. Branham, M.D., Senior Pathologist, National Institute of Health. Discussion: Oscar B. Hunter, M.D.

Wednesday, November 17: No meeting.

Friday, November 19: Joint meeting with the Baltimore City Medical Society at 1211 Cathedral Street, Baltimore.

1. "Typhoid Types of Fevers: Frequency and Problems in Diagnosis." Illustrated. Charles R. L. Halley, M.D. Discussion: Rollo E. Dyer, M.D., United States Public Health Service.
2. "Endobronchial Tumors: Diagnosis and Treatment." Illustrated. Edgar W. Davis, M.D.
3. "Recent Advances and Trends in Radiology." Arthur C. Christie, M.D., President, Fifth International Congress of Radiology.

Wednesday, November 24: Thanksgiving eve—no meeting.

ACTIVITIES OF SECTIONS

The Section on Internal Medicine will furnish the program for the Society's meeting on the evening of February 16, 1938.

"Anemia: Etiology, Diagnosis and Treatment." George R. Minot, M.D., of Boston.

Mark the date on your calendar. This is one of the fine programs the Section has had the extreme pleasure and good fortune to obtain.

The Section on Gastro-enterology, now in the process of organization as a unit of the Society, met in the Library of the Society's Building on October 11. The program:

1. "Proctological Diseases." Benjamin F. Dean, Jr., M.D.
2. "Gastroscopic Studies." Fred A. J. Geier, M.D.
3. "The Medical Management of Cholecystic Disease." William J. Mallory, M.D.
   Discussion: W. W. Sager, M.D.; and Louis Hamman, M.D., of Baltimore.

The officers are as follows:

Matthew White Perry, *Chairman*
Fred A. J. Geier, *Vice Chairman*
R. Lyman Sexton, *Secretary-Treasurer*

NEWS AND PERSONALS

Marihuana Tax Act of 1937, effective October 1, 1937, is an Act passed by Congress, signed by the President on August 2, which requires the taxing of the profession for privilege of using or prescribing the drug. Marihuana is, for the purposes of the Act, made to include "all parts of the plant Cannabis sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds, or resin." Certain proprietary medicines are affected. A number of drug firms have announced the discontinuance of the drug in their preparations. Any quantities of the drug on hand in physicians' offices must be destroyed or a tax will be applied.

Physicians Are Victimized in Instrument Deal. Reappearing in Washington, after a lapse of a few years, is the man who "plates, and repairs instruments, making them look good as new at a ridiculously small cost." He is described as being white, 5 feet 4 inches, 110 pounds, thin features, clean face, sandy hair slightly gray, wears rim spectacles, blue suit, brown fedora hat. He recently came into the office of one of our members and said he had quite a progressing business (sic) in the past 4 years, repairing, plating and sharpening scissors for physicians for 25 cents each, finishing them in first class condition. A quotation from a communication from the latest victim is as follows: "He did not look like a swindler or wise guy, in fact he was very plain and I fell completely. I gave him 9 pairs of scissors and 1 pair of needle forceps. He said they would be back in 4 days." Of course, the instruments were never returned. All should take notice. If this man appears in your office, detain him, notifying the detective headquarters.

The George Washington University School of Medicine Annual Faculty Address, at the opening session, was delivered on September 22 by Professor Francis Randall Hagner, Executive Officer of the Department of Urology. Dr. Hagner spoke on "The Early History of the George Washington University School of Medicine." He was presented to the Faculty and students by Dean Earl B. McKinley, who recently returned from Sabbatical leave spent in the Orient doing research on tropical diseases. New members of the teaching staff were announced as follows:

Robert Custis Grubbs, A.B., M.S., M.D., Instructor in Physiology; Gail Lorenz Miller, M.A., Ph.D., Instructor in Biochemistry; Leland O. W. Moore, M.D., Professor of Military Science and Tactics; Edgar Deucher Griffin, A.B., M.D., Clinical Instructor in Psychiatry; Zigmond Meyer Lebensohn, M.D., Clinical Instructor in Neurology; Joel Norton Novick, M.D., M.Sc., Clinical Instructor in Otorhinolaryngology.

The Georgetown University Brain Research Institute. On September 10 the Georgetown University School of Medicine established an institute for the investigative study of the brain. This Institute will be known as the Georgetown University Brain Research Institute and will be under the direction of Dr. Othmar Solnitzky, Professor of Anatomy, with Dr. Francis J. Warner as assistant director. A comprehensive program of neurological research work will be launched along the four following directions:

1. A complete study of the brains of vertebrates from the cyclostomes to the primates.
2. A thorough study of the development of the human brain with special regard to its morphology, nuclear masses, and fiber tracts.
3. Experimental study of the function of the various nuclei and fiber tracts of the brain by means of Marchi degeneration and retrograde cell degeneration.
4. A comprehensive study of the neuropathology of the human brain.

The Institute already possesses a large collection of animal and human brains, many of which are sectioned and stained. The instrumentarium will include, among others, the Horsley-Clarke stereotaxic instrument, the Vogt-Sartorius brain microtome, celloidin and paraffin microtomes, a specially constructed brain macrotome, cold electric cautery, moving-picture camera, microphotographic camera, and dissection microscopes. The Institute will also have two full-time specially-trained technicians, a photographer, and an artist. A large library of books, monographs, and reprints covering every phase of the projected research is available. A modern and well-equipped animal experimental laboratory is being built.

All the facilities of the Institute will be made available to all those interested in any phase of brain research. Individual desks and microscopes will be placed at the disposal of investigators.

Contributions of animal and human brains, both normal and pathological, as well as reprints of all neurological publications, will be gratefully accepted and duly accredited.

The George Washington University Medical Society held its initial meeting on Saturday, October 16, 1937. Program:

1. "Introductory Address." Cloyd Heck Marvin, President of the University.
2. "A Welcome to Earl B. McKinley, Dean of the School of Medicine." Sterling Ruffin, M.D., Professor of Medicine, Emeritus.
3. Response, with "A Review of Recent Investigations on Leprosy in the Orient." Earl B. McKinley, Dean.

The Washington Academy of Surgery held its first meeting of the year on October 8, 1937, at the Cosmos Club. The guest speaker was Arthur M. Shipley, M.D., Professor of Surgery, University of Maryland, Baltimore; subject: "Surgery of the Biliary Duct Apparatus." The new officers for the year 1937–1938 are as follows: Drs. James A. Cahill, Jr., *President;* Daniel L. Borden, *Vice President;* F. C. Fishback, *Secretary-Treasurer.*

The meetings are held on the second Friday of October, December, February and April. Dr. Isaac A. Bigger, Professor of Surgery of the Medical College of Virginia, Richmond, will be the guest speaker for the December meeting; subject: "Surgery of the Heart and Pericardium."

The Annual Public Meeting and "Health Crusade" of the District of Columbia Tuberculosis Association will be held Tuesday, November 22, 1937, at 8 P.M., in the auditorium of the United States Public Health Service. Symposium: "How to Protect Your Home Against Tuberculosis." Dr. J. Arthur Myers of Minnesota, President of the National Tuberculosis Assocation, will discuss the topic "Modern Methods in the Control of Tuberculosis." Other speakers and topics include: "The High Incidence of Tuberculosis Among Negroes," C. St. C. Guild, M.D., Field Secretary of the National Tuberculosis Association, New York City; "Milestones Toward Adequate Hospitalization for the Tuberculous in the District of Columbia," James G. Townsend, M.D., President, District of Columbia Tuberculosis Association. Mrs. Ernest R. Grant, Managing Director, District of Columbia Tuberculosis Association, will preside. All interested persons are invited to attend.

Clinical Club of Washington announces the following officer personnel for 1937–1938:

H. N. Dorman, President
William P. Herbst, Jr., Vice President
Harry S. Bernton, Secretary-Treasurer

Executive Committee:
Coursen B. Conklin
L. Brison Norris
Officers, *ex officio*

Southern Medical Association meets in New Orleans, November 30–December 1–2–3. Active Members of the Medical Society of the District of Columbia may become members of the Southern Medical Association on application. A number on the Medical Society of the District of Columbia roster will appear on the program. Prepare now to go to add to your medical knowledge from the vast fund in the scientific exhibits and papers, and to enjoy the well-known entertaining features of the Crescent City.

Annual Scientific Assembly, May 4–5, 1938. The Society, in session on the evening of October 6, 1937, voted to authorize and direct the President to appoint appropriate committees in preparation for this meeting. Note the dates. Make your plans for participation now.

Raymond Thomas Holden, M.D.
(1860—1937)

In the passing of Dr. Raymond T. Holden, Sr., the Medical Society of the District of Columbia has lost a member who had been on the rolls since April 1, 1885. His membershp in the Medical Association of the District of Columbia dated from May 9, 1883. Only one other member now on the rolls antedates his entrance into the Society. On January 1, 1929, he became a Life Member.

Dr. Holden at an early age became active in Society affairs, serving as a member of the important Board of Censors, 1886–1887. Successively he served on the Committee on Public Health, 1898–1901; Committee on Printing History, 1906–1911; Committee on Red Cross Work, 1915; Executive Committee, 1916–1918; Building Committee, 1921–1923; Committee of Censors, 1929–1930; also First Vice President, 1914. He was a native Washingtonian, the son of Thomas and Catherine Gleeson Holden. His early education was obtained in St. John's College, later in 1881 receiving his degree in medicine from Georgetown University School of Medicine. Through his medical acumen and fine personality he developed a large practice to which he gave his services until the day of his death. He served on the staff of Providence Hospital for a number of years.

Dr. Holden married Celeste Selma Moritz on October 7, 1896, by whom he is survived. He is also survived by two daughters, Mrs. Len J. Dillon of Detroit, and Mrs. Fred J. Murphy of Boston; and two sons, William J. Holden, and Dr. Raymond T. Holden, Jr., the latter a member of this Society. His funeral, attended by many of his former fellow-members, was held Tuesday, October 19, 1937, at the Shrine of the Sacred Heart. Honorary pall-bearers included: Drs. J. Rozier Biggs, James A. Cahill, Jr., C. N. Chipman, C. M. Hammett, J. Thomas Kelley, Jr., Thomas S. Lee, Frank Leech, C. C. Marbury, William Gerry Morgan, J. J. Mundell, L. Brison Norris, Frederick O. Roman, Sterling Ruffin, H. R. Schreiber, William M. Sprigg, Millard F. Thompson, Joseph S. Wall and Charles Stanley White.

MEDICAL ANNALS
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THE PRESENT STATUS OF TUBERCULOSIS IN THE DISTRICT OF COLUMBIA*

GEORGE C. RUHLAND, M.D., *Health Officer*, AND C. C. DAUER, M.D., *Epidemiologist*,
District of Columbia Health Department

Tuberculosis remains as one of the important public health problems in the District of Columbia as well as in other communities of this country. The disease continues to be one of the important causes of death among young adults. Because of this fact, medical, economic and social considerations still demand our whole-hearted attention.

This presentation of the present status of tuberculosis in the District of Columbia can touch upon certain high points only. A complete analysis could not be reported in a short period of time, nor can all details be included. It will be necessary to depend principally upon mortality data because they are more nearly complete. It should be pointed out here that no correction has been made for non-resident deaths from the disease. Examination of data available for the past 2 years revealed that non-resident deaths from tuberculosis have about equaled the number of deaths of residents outside the District of Columbia. Important as morbidity data are in the analysis of the problem, they are too incomplete to warrant any sweeping conclusions. They do, however, illustrate how certain phases of the problem need to be emphasized or approached.

In comparison with the entire country, tuberculosis death rates in the District of Columbia are higher in most respects. Since 1930 the average mortality rate for the Registration Area has been slightly over 60 per 100,000 population, while that for the District of Columbia has been about 115. When these data are broken up into rates by sex and color, the rates for the District of Columbia still suffer by comparison. White male rates have been 20 per cent higher; white female rates 20 per cent lower; colored male rates 43 per cent higher; and colored female rates 32 per cent higher in the District of Columbia than for the country as a whole.

To understand the present status of tuberculosis in the District of Columbia, one must compare current conditions with those of the past, because changes in prevalence take place slowly. The trend of mortality here has been progressively downward since 1875 (Fig. 1 and Table 1), which is quite similar to the trend in other communities for which we have comparable data. Because of the large percentage of Negroes in the population of the District of Columbia, trends of white and colored persons are presented separately. The trend of tuberculosis death rates for white persons has been steadily downward, a 72 per cent reduction since 1900. This is similar to the amount of decline in the Registration Area. The trend for the colored population is quite different. From 1875 to 1920 there was a marked reduction in mortality with some fluctuation from decade to decade, but since 1920 there has been little or none. In this respect the trend of mortality for colored persons in the District of Columbia has not been different from that for the colored population in New York City. The failure of the Negro death rates to decline in the past 15 years probably is the result of several factors, none of which we can clearly define at this time due to lack of reliable information.

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* Read before the Society, October 27, 1937.

The ratio of white to colored mortality rates has undergone marked changes. Whereas, previous to 1900 the ratio was 1 to 2, it has gradually changed to about 1 to 5. This has been brought about by a more rapid decline of mortality among white persons. It indicates that tuberculosis among colored persons is becoming relatively more important in the District of Columbia.

The trend of mortality for each race by age groups is consistent with the data for all ages. In general, the decline in mortality has been the same for white and colored persons under 10 years of age in the District of Columbia, about 75 per cent reduction since 1900 (Table 2). In persons over 10 years of age, the decline in mortality has been greater among white persons, between 65 and 75 per cent for white and 40 to 50 per cent for colored persons.

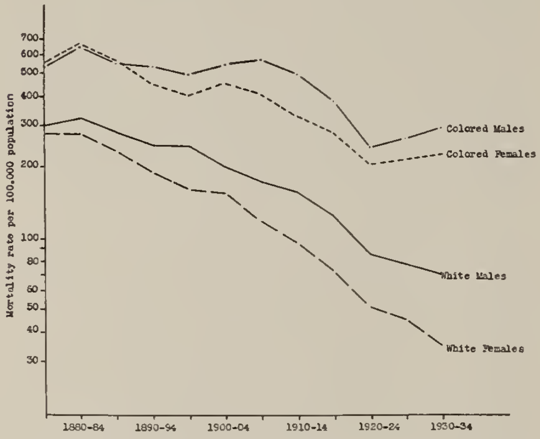

Fig. 1. Trend of Mortality from Pulmonary Tuberculosis in Washington, D. C., from 1875 to 1934.

Mortality rates for white females now reach their peak in the young adult ages between 30 and 39 years, with a secondary rise in old age. Among white males mortality rates at the present time gradually increase after 10 years of age and reach their peak in old age, 60 years and over. The peak of mortality for colored males and females is reached in the 20- to 29-year group. Among females the mortality decreases rapidly after 30 years, while the male mortality remains at quite a high level.

The greatest amount of change in the age distribution of tuberculosis mortality has occurred among white females. The high mortality in old age has to a great extent been eliminated. Among white males and in colored persons the general curve of age distribution has been essentially the same for many decades, i.e., the decline has been about the same in each age group.

The difference in mortality at the present time among white males and white females is quite marked. The ratio of male to female rates from 1930 to 1934 was 1.93 to 1, or about twice as many deaths among males as females per 100,000 of population. In this respect Washington is similar to other large cities, particularly those in the northeastern section of the country. The higher rates among males is an important point to remember in planning any control program against the disease. Among colored persons the sex differences have been less marked, the male rates exceeding the females by about one third.

TABLE 1

Mortality Rates from Pulmonary Tuberculosis in Washington, D. C.

YEARS	WHITE		COLORED	
	Male	Female	Male	Female
1875–79	300.4	272.0	533.8	558.8
1880–84	322.0	271.5	644.0	677.5
1885–89	280.5	233.8	550.0	561.3
1890–94	245.5	190.3	538.5	446.7
1895–99	242.2	160.6	489.3	400.0
1900–04	201.8	153.0	540.0	452.0
1905–09	172.6	117.9	569.5	404.7
1910–14	155.7	94.7	496.6	328.3
1915–19	122.4	72.1	380.6	278.0
1920–24	84.1	50.5	244.4	205.0
1925–29	77.7	44.6	262.2	215.0
1930–34	69.6	34.0	292.9	228.7

A discussion of the tuberculosis problem in the District of Columbia must include social and economic conditions of those who die of tuberculosis. Since 1930, 34 per cent of white male deaths have occurred among those whose occupation can be classified as the manufacturing or mechanical trades. This group consists, for the most part, of the low-income, laboring group. In 1930 they comprised 18 per cent of the total white male population in the District of Columbia. Another group, clerks, which are made up of what we might classify as the middle-income group, who are principally Government employees, furnished 12 per cent of white male tuberculosis deaths. They comprised 12 per cent of the population in 1930. Other groups, smaller in number, furnished smaller percentages of the total number of deaths. It seems apparent from these data that, insofar as the white male population of Washington is concerned, about one fifth of the white males who are in the low-income group furnish one third of the deaths. This fact needs to be more clearly recognized in our attack on the disease.

TABLE 2

TUBERCULOSIS DEATH RATES IN WASHINGTON, D. C., BY AGE, SEX, AND COLOR, AND PERCENTAGE DECREASE IN RATES FROM 1900 TO 1930

AGE GROUP YEARS	1900	1910	1920	1930	PER CENT DECREASE 1900 TO 1930	1900	1910	1920	1930	PER CENT DECREASE 1900 TO 1930
	White Male					Colored Male				
0-4	138.2	106.1	57.7	30.0	78.3	750.0	380.0	273.7	260.0	65.4
5-9	22.2	30.4	18.8	8.0	63.6	188.6	225.0	68.3	52.8	72.0
10-19	76.8	44.8	31.9	13.5	82.4	400.0	377.0	226.5	182.6	54.4
20-29	284.3	169.3	124.1	60.0	78.9	765.0	771.0	421.8	375.0	51.0
30-39	336.6	282.0	150.0	117.1	65.2	661.0	805.0	452.1	369.2	44.2
40-49	303.0	272.8	149.0	131.4	56.6	609.0	723.0	387.4	393.1	35.5
50-59	294.2	241.6	159.1	143.1	51.4	633.0	682.0	302.3	292.6	53.8
60-69	365.4	200.0	174.0	142.6	61.0	560.0	571.4	364.7	270.0	51.8
70 and over	368.5	244.7	153.5	140.0	62.0	368.0	460.0	282.3	252.6	31.4
	White Female					Colored Female				
0-4	146.1	120.8	50.0	24.0	83.6	751.0	400.0	140.0	176.0	76.6
5-9	29.5	31.3	16.7	9.1	69.2	256.0	184.0	51.1	43.6	83.2
10-19	90.1	60.2	45.5	21.1	76.6	469.0	423.0	330.6	267.2	43.0
20-29	254.4	166.5	72.2	58.3	77.1	600.0	554.0	385.3	378.6	44.2
30-39	237.1	145.3	77.0	71.7	69.7	509.0	480.0	268.3	248.4	51.2
40-49	184.3	108.3	70.2	42.1	77.2	436.0	305.0	166.2	152.4	65.1
50-59	174.7	147.5	80.0	54.0	69.1	300.0	230.0	175.0	155.0	48.3
60-69	283.5	104.0	81.7	60.0	78.8	353.0	163.3	113.0	154.0	56.4
70 and over	218.0	152.4	78.7	81.0	62.9	300.0	116.5	124.6	128.0	57.4

Approximately 25 per cent of the tuberculosis deaths in white females reported since 1930 were among those who had some form of occupation outside of the home. In 1930 employed females constituted 32 per cent of the white female population of the District of Columbia. This would seem to indicate that tuberculosis is not any more frequent, judging by mortality data, among stenographers, clerks, and other employed women than among housewives. It is reasonable to suppose that working women probably have more of the necessities of life than do many women who remain at home doing housework. This would not necessarily apply to all housewives.

Most employed Negro males are in the low-income groups, and as would be expected, most deaths among male Negroes occur among those whose occupations are listed in the low-income laboring class. About 60 per cent of all female colored deaths from tuberculosis were among those classified as domestics, maids, and various other personnel services. This 60 per cent of deaths occurred among those who at some time had been employed in the homes of the better-class white population in the District of Columbia. They probably have been a source of infection to children and other susceptible persons in many instances.

Time will not permit a detailed examination of the geographic location of deaths from tuberculosis in the District of Columbia. By far the majority of persons who die of tuberculosis have resided in the densely populated district from New Hampshire Avenue east to the Anacostia River, and from Florida Avenue south to the Potomac River. Not only is the number of deaths greater in this area, but also death rates. Even mortality rates for the white population are higher in this area than for other sections. It is a section where there are to be found large numbers of the low-income classes of people and where housing conditions are far from ideal. Such conditions are always favorable for high incidence and death rates from tuberculosis and other infectious diseases.

The information concerning the actual cases of tuberculosis in the District of Columbia is in a very unsatisfactory state. Many cases are not reported until the time of the patient's death. Many are not diagnosed until late in the course of the disease. Failure to diagnose may be due to the fact that the disease is not recognized by the physician or perhaps because the patient postpones medical consultation, or both. Some physicians may not report cases of tuberculosis for fear of some interference on the part of the Health Department or for fear that the information may be made public. Both of these fears are without foundation. All information regarding a report of any disease is regarded as strictly confidential.

In 1936 more than one half of all cases reported by physicians, clinics, hospitals and other institutions reported the disease to the Health Department at the time of death. The percentage reported late by private physicians is even greater. This condition is not one of which anyone may be proud. It can not be excused merely on the plea that most patients consult their physicians just before they die of the disease, because colored patients on the average live about 6 months after entering sanatoria, and white persons on the average live 1 or more years following hospitalization. Reporting cases promptly would in many instances be a stimulus for enlisting the aid of the Health Department or other agencies in securing hospitalization and perhaps in securing the much needed assistance for other members of infected families.

In the past year, there were examined in the Health Department Tuberculosis Clinic about 1,300 new white patients, and approximately 1,800 colored patients. Of these, 10.7 per cent of the white, and 18.4 per cent of the colored patients had some form of tuberculosis. About 20 per cent of the white and colored cases were in the minimal stage. Thirty-four per cent of the white cases were in the far-advanced stage, and 46 per cent of the colored cases were in a similar stage. Such conditions are not favorable for the most effective control, nor for the most favorable results with the newer methods of treatment.

The problem of control of tuberculosis in the District of Columbia means more than the building of a sanatorium, such as the one just completed at Glenn Dale. Cases must be diagnosed early to prevent long continued contact with other members of the household. This means that the public must be taught the essentials of tuberculosis prevention, the early signs of the disease, and the value of prompt treatment. The medical profession must also become more tuberculosis minded; it must have a better appreciation of the natural history and development of the disease and develop a greater acumen for diagnosis in the early stages. Tuberculosis must be reported as soon as discovered so that all necessary agencies may be mobilized for hospitalization or other care, and proper treatment of the case. Finally, there needs to be more attention to (1) earlier diagnosis of contacts, (2) helping the patient and his family to adjust the family problems so that fewer patients leave the hospital against advice, (3) keeping a watchful eye on patients after discharge so that fewer breakdowns will occur, and (4) tying already existing facilities together for a better year-round tuberculosis control program.

Summary

In summing up the present status of the tuberculosis problem in the District of Columbia, the following points should be emphasized:

1. Tuberculosis mortality is decreasing more rapidly among white than among colored persons. Colored mortality has been stationary since 1920.
2. Mortality is about twice as high among white males as white females. Mortality among colored males is only slightly higher than for colored females.
3. The lower-income classes among white males furnish one third of the white male tuberculosis deaths. Employed white females do not appear to have a higher mortality than housewives in general. A large proportion of colored females who die of tuberculosis have been employed in homes of the white population.
4. Reporting of cases of tuberculosis is in a large majority of instances delayed until the patient dies or is about to die.
5. Discovery of tuberculosis is not made until the disease has reached the far-advanced stage in a large percentage of cases.

MEDICAL USES OF ERGOTAMINE TARTRATE*

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Ergotamine† is a delicate alkaloidal principle of ergot and one of the active constituents upon which this drug depends for its therapeutic usefulness. It is available in the form of the tartrate salt and has been used successfully for a number of years as a uterine stimulant and for the prevention and treatment of postpartum complications. More recently it has been employed for treatment of migraine, pruritis, hyperthyroidism, glaucoma, autonomic instability, cord bladder, and other conditions. Its effectiveness in relieving migraine is now widely known.

The two important known physiological effects of ergotamine are the stimulation of smooth muscle organs (uterus, arteries, etc.) and inhibition of the myoneural junctions of the sympathetic nervous system. In this latter action Rothlin states that ergotamine behaves toward the sympathetic as atropine does toward the parasympathetic, but Cushny says that the inhibitory action of ergotamine on the sympathetic is elicited only by large doses and does not occur in the therapeutic use of ergot. There is growing clinical evidence that sympathetic inhibition is obtained from therapeutic doses of ergotamine in patients having sympathetic overactivity, although the same results may not occur in normal individuals.

The experimental studies of Youmans, et al., indicate that ergotamine depresses certain functions of the sympathetic, but only when these are stimulated, and that this depressing effect is directly proportional to the degree of sympathetic excitation. Further in this connection, O'Sullivan suggests that the effectiveness of the alkaloid varies with the chemicals and hormones circulating in the blood, basing this hypothesis partly on the fact that obstetrical patients react to the drug differently and with fewer untoward results than patients with migraine. Von Storch believes that the beneficial effect of ergotamine in migraine is closely associated with its vasoconstrictor action on the dural and temporal arteries, dilatation of which he thinks is common to all cases of migraine.

Most physicians are familiar with the indications and uses for ergot derivatives in obstetrical and gynecological conditions. It is not the purpose of this paper to review this subject, but to present the medical uses of ergotamine tartrate.

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* Read at the Second Annual Alumni Extension Course of Georgetown University School of Medicine.

† Gynergen (ergotamine tartrate).

MIGRAINE

In cases of typical migraine the diagnosis is usually not difficult. There is a history of similar attacks over a period of years, alternating with symptom-free intervals. The individual seizure lasts 24 to 48 hours and is characterized by an aura most often visual in type, uncontrollable headache, prostration, nausea and vomiting; cessation of symptoms and rapid recovery end the episode. Atypical migraine, however, is much more common than the classical form and frequently presents a difficult diagnostic problem. Since the recognition of the effectiveness of ergotamine for the symptomatic relief of migraine, the drug has often been used as a therapeutic test of the diagnosis.

As a rule, the earlier in an attack the drug is given, the smaller the dose necessary for relief and the greater benefit it will be to the patient. To prevent the full development of a seizure an initial dose of 0.25 mg. to 0.5 mg. (0.5 cc. to 1 cc.) should be injected intramuscularly or subcutaneously and repeated after 1 or 2 hours if necessary. If oral dosage is to be tried an initial quantity of 3 to 6 mg. (3 to 6 tablets) should be given, followed at hourly intervals by 1 or 2 additional tablets until a total of 10 or 12 have been taken or relief has been obtained.

When it is possible to observe patients in a series of attacks the dose of ergotamine and the method of giving it should be varied for each patient to find the smallest amount of the drug that will be effective and the most suitable way of giving it. In subsequent attacks this dosage should be used, although in severe episodes the quantity given may have to be increased. While vomiting may preclude the possibility of good results with oral dosage, nevertheless, this mode of administration often is quite satisfactory in mild cases and when employed before emesis starts. In this connection, Kelly reported excellent results following sublingual dosage. He found 1 or 2 tablets given this way equal to 5 or 6 when ingested. It may be practical to instruct the patient who does not respond to medication by mouth in self-administration of the drug by injection, provided, of course, that he can be made to understand the dangers of overdosage and the importance of remaining under medical supervision.

According to all reported experience these doses are safe in cases in which there are no specific contraindications to the use of ergot. Von Storch warns, however, that they should not be exceeded in a 12-hour period by those not familiar with the drug.

The effectiveness of ergotamine tartrate in relieving the migraine syndrome is little short of miraculous. Given by injection the drug afforded relief to 92 per cent of the patients in O'Sullivan's series of 97 cases. In this same study 69 per cent of the patients were relieved by oral dosage. Lennox and von Storch reported abrupt and complete relief in 90 per cent of 109 migraine patients who received the drug by injection; the time required to check an attack varied from 15 minutes to several hours. Oral administration afforded relief more slowly (1 to 8 hours). The use of the drug during the symptom-free interval apparently is not an effective prophylactic of attacks. The efficacy of ergotamine does not decrease with repeated use.

It is not unusual for ergotamine to produce minor uncomfortable symptoms in migraine patients. The common reactions are nausea and vomiting, sensations of burning and tingling of the fingers and toes, muscle pains, stiffness of joints, a sense of constriction in the throat, and weakness. Unusual and infrequent effects are delirium, diarrhea, and fever. Rarely, symptoms caused by the drug are so distressing that the patient prefers the headache to the treatment.

The nausea and vomiting produced by the alkaloid are usually mild, but when annoying can often be relieved by the hypodermic injection of 1/150 grain of atropine sulphate. The other minor untoward effects are usually quite transient and require no special treatment.

When muscle pains are severe they can be relieved by the intravenous administration of 10 cc. of 10 per cent calcium gluconate, and O'Sullivan states that their recurrence may be prevented by daily oral calcium therapy.

PRURITUS

Generalized pruritus occurring in cases of jaundice and uremia can be distressing, and often proves intractable to the usual measures for relief of pruritus. Believing that this symptom results from increased irritability of sympathetic nerve endings due to the action of some toxin and because ergotamine tartrate is a sympathetic depressant, Lichtman used this drug in 4 such cases, which he reported in 1931. He administered 1 mg. orally 3 times daily. Whether or not his reasons for using ergotamine were sound, the therapeutic effect was excellent. Later, Snell and Keyes reported that ergotamine is by far the best therapeutic means for relief of pruritus in jaundiced patients. They found oral administration of 1 mg. 3 or 4 times daily to be satisfactory in most cases, but in a few resistant cases subcutaneous injection of 0.5 mg. was employed daily or twice daily.

It should be remembered, however, that patients with pruritus of the type described are in a toxic state and not altogether suitable subjects for medication with active drugs. Consequently, ergotamine should be used cautiously, preferably by oral dosage. If the drug is to be effective, relief from itching is obtained quickly and lasts 1 to 8 hours, occasionally longer. Prolonged administration of ergotamine for pruritus is not warranted. Snell and Keyes, and Lichtman made no record of minor symptoms being provoked by ergotamine, nor have we observed such symptoms in patients who have received the alkaloid for this purpose at Georgetown University Hospital and in private practice. Yater and Cahill have reported a case of gangrenous ergotism due to ergotamine tartrate used for pruritus of jaundice due to toxic hepatitis; in this case excessive doses of the drug were used. Gould, Price and Ginsberg have made a similar report; in their case overdosage was not a factor, but a specific contraindication to use of the drug existed.

HYPERTHYROIDISM

Adlersberg and Porges reported the results obtained in 13 of a group of 22 patients with hyperthyroidism, treated with ergotamine in 1924–1925. The remaining 9 patients could not be followed up. The treatment induced nearly complete recovery in almost all. The only residual symptoms found were a tendency to emotional tachycardia, slight exophthalmus and mild nervous irritability. The authors believe that these symptoms are commonly seen in such cases after any form of treatment. They recommend the oral administration of ergotamine in preference to its hypodermic or intravenous injection, since equally satisfactory results can thus be obtained. They suggest an oral dose beginning with 3 mg. per day, increasing up to 3 to 4 mg. 3 times a day. This dose is then diminished progressively, and, after 2 or 3 weeks of treatment, the drug should be given intermittently for from 1 to 3 weeks, following which it is administered as necessary to control the symptoms.

Mercke recommends ergotamine in both operative and nonoperative cases of hyperthyroidism. This drug, he found, reduces the basal metabolism, controls tachycardia and other symptoms due to sympathetic stimulation. When used before operation it improves the general condition of the patient and lessens the operative risk. In one patient the heart rate was reduced from 160 to 60 beats per minute, while in another the reduction was from 160–170 to 110–120. The results surpassed those with any other drug.

Porges administered 2 to 3 mg. daily to hyperthyroidism patients for periods of 2 to 3 weeks. He found that there was a general quieting influence with relief from insomnia. Further, he says that considerable improvement often results, although complete recovery does not follow a short course of treatment. On the other hand, he observed in many cases a disappearance of all symptoms after intermittent treatment continued over periods of from 1 to 2 years, only a certain degree of exophthalmos persisting.

In paroxysmal auricular tachycardia Oppenheim found the slowing effect of ergotamine upon the heart rate to be quite as effective as in hyperthyroidism. He states that subcutaneous injection of 0.5 mg. (1 cc.) of ergotamine tartrate during attacks causes prompt cessation of the seizure.

While the reported effects of ergotamine in hyperthyroidism appear beneficial, there has been no further clinical confirmation of this work, nor is there physiologic evidence at the present time to support strongly the idea that the drug will prove generally useful in this condition.

GLAUCOMA

Gifford in a discussion of this condition before the Canadian Medical Association, June 20, 1934, emphasized that most cases of glaucoma, and especially primary glaucoma, sooner or later require surgical intervention. With appropriate medical treatment, however, it may be possible to postpone surgery and even avoid it entirely.

In secondary glaucoma treatment will in most cases depend upon the cause. In iritis with secondary rise of tension, he believes that paracentesis, repeated after several days if necessary, will often keep the tension within safe limits until the inflammation is controlled by treatment directed against the cause. As a drug to reduce intra-ocular tension, Gifford recommends ergotamine tartrate and injects 0.25 mg. subcutaneously twice daily for a few days. He regards oral administration as less effective but suggests 2 to 3 mg. daily. The drug acts by paralyzing the sympathetic endings in the eye, thus reducing the permeability of the blood vessels of the uveal tract and decreasing the secretion of the ciliary body. Following injections, he states that he has seen falls in tension from 30 to 18, 37 to 17, 35 to 20, and from 40 to 25 mm. In chronic glaucoma ergotamine is impractical for obvious reasons.

AUTONOMIC INSTABILITY

Although pharmacologic studies seem to demonstrate that therapeutic doses of ergotamine tartrate have little or no inhibitory effect on the sympathetic nervous system, some clinicians believe that this view must be modified in cases in which there is sympathetic overactivity. Such overactivity may be found in patients who are variously described as nervous, neurotic, psychoneurotic, sufferers of autonomic instability or neurovegetative dystonia, etc.

Orsi and Bravetta studied the effects of ergotamine on such patients and reported a beneficial influence of the drug on the manifestations of increased tonus of the sympathetic nervous system. Similar quantitative studies have since been reported by Jores and Goyert for a combination of ergotamine tartrate with belladonna alkaloids and phenobarbital.* Still others have extended these clinical researches, using ergotamine or the ergotamine-belladonna-phenobarbital mixture for such things as menopausal symptoms, epilepsy, psychogenic headache, and tic douloureux. It cannot be denied that ergotamine alone or in combination with other drugs may have had a beneficial effect in the cases reported in all these studies. However, critical analysis reveals that none of the studies was conducted with the same view to answering objections that has characterized, for example, the research of O'Sullivan and her coworkers on the use of ergotamine for migraine.

A further extension of the use of ergotamine for autonomic instability has been its application for symptoms of such instability in psychotic patients. Baber and Tietz reported a series of 62 patients who were given ergotamine tartrate orally in doses as low even as 1 mg. daily in some cases for periods ranging upward to 4 months. In many cases the patients showed marked improvement, losing destructive, homicidal, or suicidal tendencies and gaining appreciation of environment. Benefit was greatest in manic depressive psychoses, but the schizophrenic group also showed a significant percentage of improvement. These results are interesting in view of the fact that injections of epinephrine are known to aggravate the very symptoms which ergotamine improves in these patients.

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* Bellergal (each tablet contains 0.0001 Gm. 1-rotatory belladonna alkaloid, 0.0003 Gm. ergotamine tartrate, and 0.02 Gm. phenobarbital).

Leonhard, in 1932, reported the successful use of ergotamine in the treatment of an extensive series of melancholia patients. Those responding best were typical cases of melancholia with inhibitions. Subsequently, and based upon his previous experience, he employed ergotamine in quiet inhibited depressions and found that improvement in behavior took place so regularly in conjunction with medication that the efficacy of the drug could hardly be questioned.

CORD BLADDER

Gernon, Palmer and McKenna, in 1936, reported the use of ergotamine tartrate for the treatment of tabetic bladders. Later (1937) Palmer and Gernon wrote more fully on the same subject, adding illustrative cases. The drug was used to inhibit the sympathetic innervation of the bladder, thereby allowing relaxation of the internal sphincter and contraction of the detrusor muscle. It was their belief that the stimulating effect of the sympathetic on the vesical sphincter plays an important rôle in maintaining overdistention of the tabetic bladder.

The average dose of ergotamine recommended by these authors is 4 mg. daily by mouth. Their studies support the conclusion that this is the drug of choice for this condition. While all cases in their series were improved subjectively, loss of beneficial effect tends to appear at varying intervals after cessation of treatment. At such times it becomes necessary to renew administration of the drug. Improvement is marked by restoration of the sensation of bladder fullness, regained continence, and diminution of frequency with increase in force of urination.

DANGERS OF ERGOTAMINE TARTRATE

No discussion of the therapeutic value of ergotamine tartrate is complete without reiteration of the warnings concerning potential dangers of the drug. Both the Council on Pharmacy and Chemistry of the American Medical Association and the manufacturers of the drug have repeatedly called attention to its possible toxic effects.

The two cases of gangrenous ergotism reported by Yater and Cahill, and by Gould, Price, and Ginsberg include complete reviews of the literature on the subject of severe toxic effects of ergotamine. These two reports lead to the following conclusions:

1. Ergotamine tartrate should not be used without a thorough knowledge of its dosage, the variation of this dosage according to routes of administration, and the specific contraindications to its use.

2. Ergotamine tartrate is specifically contraindicated in cases of occlusive vascular disease and cases of puerperal sepsis. There is some support to the beliefs that it is contraindicated in cases of severe toxemia from any cause and that its prolonged administration should be only at the hands of those experienced with the drug.

One other warning is worthy of mention. Von Storch calls attention to the fact that the almost perfect reliability of ergotamine for relief of migraine may tend to cause the therapeutists to neglect thorough search for a possible cause of the migraine syndrome in a given patient. Obviously, purely symptomatic relief by means of ergotamine is not the goal in treatment of this condition.

SUMMARY

1. Ergotamine tartrate stimulates smooth muscle organs and inhibits the sympathetic nervous system. This latter effect apparently occurs with therapeutic doses of the drug.

2. Results of the use of ergotamine by a number of workers for migraine, pruritus, hyperthyroidism, glaucoma, autonomic instability, and cord bladder are given.

3. Potential dangers of ergotamine and its contraindications must always be kept in mind.

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ABSTRACT OF PAPER READ BEFORE THE SOCIETY

"Serum Therapy in Pneumonia,"* **Francis G. Blake, M.D.**, New Haven, Connecticut.

During the 25 years which have elapsed since Cole presented his first communication on pneumococcus infection and immunity, a steadily progressive advance in knowledge concerning pneumococcal pneumonia and its treatment with specific serums has taken place. Although it had been clearly demonstrated by 1920 through the efforts of Cole and his collaborators that serum was effective in curing lobar pneumonia in man, and by Cecil and Blake in experimental animals, the general acceptance and application of serum therapy was handicapped by the fact that a therapeutically valuable serum was available only for Type I infections comprising not more than 30 per cent of cases, that the serum was unconcentrated and consequently had to be administered intravenously in large volume at frequent intervals with a high incidence of fairly severe serum disease, that no technically simple and rapid method for type determination was known and no generally adequate appreciation of the necessity for early treatment existed, so that many disappointing failures in late cases fostered unjustified skepticism and discouragement.

During the last 10 years, however, a number of important advances have been made which have served to resolve or ameliorate these handicaps. Important among these advances are the development of refined and concentrated serums, largely through the work of Felton; the subdivision of the old heterogeneous Group IV pneumococci into specific types by Cooper; the finding that at least 3 of these, Types V, VII, and VIII are of significantly frequent incidence; the development of effective concentrated serum not only for Type I pneumonia but also for Types II, V, VII and VIII, so that approximately 60 per cent of cases are amenable to serum therapy; the re-introduction of the relatively simple and rapid Neufeld method for type determination; the more general appreciation that lobar pneumonia is a medical emergency permitting no delay if the best results from serum therapy are to be obtained; and finally and quite recently the development by Horsfall and Goodner of highly potent antipneumococcus rabbit serum which would appear to have a number of important advantages over horse serum. As with all serum therapy the best results will be obtained only by early treatment within 72 hours after onset and with adequate dosage, 100,000 to 400,000 units, depending upon type, duration and severity.

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THE VALUE OF COMBINING SEDATION OF THE CENTRAL AND AUTONOMIC NERVOUS SYSTEMS IN THE TREATMENT OF EPILEPSY*

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Introduction

Since the term epilepsy is used to describe the presenting symptoms in convulsive attacks from various causes, it is not surprising to find some degree of benefit attributed to many forms of therapy. By careful examination, which usually includes encephalography or ventriculography before the study is completed, evidence of pathology can be found in many instances. Patients having brain tumor or traumatic epilepsy with a cortical scar may be given the benefit of surgery. However, a large majority of patients with epilepsy either have no demonstrable abnormality of the brain or they present evidence of diffuse atrophy of the brain, and are, therefore, dependent upon medical treatment. A few are helped by glandular therapy and a few are said to respond to psychotherapy. The most widely used drugs are bromides and phenobarbital, both of which act by raising the threshold for stimuli which precipitate attacks. Another method of treatment, namely, dehydration, has been advocated by Temple Fay with the idea of improving the circulation of the brain. Undoubtedly the dehydration régime is beneficial in some instances, especially when used in combination with phenobarbital or sodium bromide.

The object of this paper is to report the results of treatment in 26 patients, most of whom were under observation for a year and a half in the Neurosurgical Follow-up Clinic at the Hospital of the University of Pennsylvania. All had been treated by the routine methods. Nearly all had had encephalograms and belonged to the groups in which surgery had nothing to offer, or in which it had been tried without relief. Several drugs acting upon the circulation directly or through the autonomic nervous system were employed, among which were ergotamine tartrate, bellafolin, ephedrine, acetylcholine, and histamine. They were used alone, in combination with each other, or with the addition of phenobarbital or sodium bromide. Before treatment was started, a patient was required to submit a list of his attacks, giving the time of occurrence and the character of the seizure. If the attacks were infrequent, a complete list since the onset or for a period of several years was obtained. If the attacks occurred several times a week, or several times a day, then a list of attacks for only a few months was required with a weekly average for a year.

Results

A. Histamine. Histamine hydrochloride, 0.5 cc. increased to 1 cc. of the 1 to 1,000 solution, was used in 6 patients. Given once or twice weekly and administered with the patient lying down, the injections caused flushing of the face and sometimes dizziness. One patient was moderately improved following this treatment for a period of 8 months, but seeing no further benefit, discontinued its use. One man, 27 years of age, had received a head injury at the age of 12 and began having convulsive attacks when he was 17. The attacks occurred at regular intervals of 3 to 4 weeks. A calcified hematoma, 5 to 6 centimeters in diameter, was removed at operation in 1933, but the attacks continued with the same regularity. Phenobarbital, 1 grain 3 times a day, had no effect. When histamine was given once a week in addition to the phenobarbital there was still no change. The use of histamine once a week, phenobarbital, 1 grain 3 times a day, and sodium bromide, 10 grains 3 times a day, as combined therapy resulted in no attacks for 6 months and only 6 attacks during the next 9 months.

B. Ephedrine. Since we had a patient under observation with narcolepsy who had been relieved by ephedrine, $\frac{3}{8}$ grain 3 times a day, this drug was tried in 3 patients with convulsive attacks. One patient was slightly improved and 2 were unimproved.

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* Read before the Section on Neurology and Psychiatry of the Society, April 15, 1937.

C. Choline. Acetylcholine, which stimulates the parasympathetic nerves, administered orally to 2 patients increased the frequency of the attacks in both.

D. Bellergal. Since a combination of phenobarbital, ergotamine tartrate and bellafolin in the form of Bellergal, the exact composition of which is given in a footnote, has been used with beneficial results in patients with various functional disturbances within the central and autonomic nervous systems, such as neuroses, vagotonia, sympathicotonia and amphotonia, it was decided to try it in the treatment of epilepsy. Experimentally, Jores and Goyert found that after the administration of ephedrine and pilocarpine, Bellergal reduced nervous excitability as determined by Aschner's ocular pressure test, the dermographism reaction, and the respiration arrhythmia test, as well as alterations in pulse rate, blood pressure and body temperature. Clinically, Silverstein believed that this preparation relaxed the spastic condition in the viscera and blood vessels so commonly present in disturbed functional states and said that it is a splendid adjunct in the treatment of psychogenic headache. Forman employed it quite successfully for the symptomatic relief of 21 menopausal patients in whom nervousness, insomnia and headache were the most annoying manifestations.

Of our series of 21 epileptic patients to whom Bellergal was given over an average period of 18 months, 4 were greatly improved, 9 were slightly or moderately improved, and 7 were unimproved. Two of the 4 patients who were considered greatly improved had no attacks during this period of observation. Four case records are herewith briefly presented to illustrate the character and frequency of attacks in those benefited by combined sedation of the central and autonomic nervous systems.

ILLUSTRATIVE CASES

Case 1: B. G., a white female, aged 16 years, had had convulsions since the age of 18 months. They started with clonic movements of the left upper extremity and soon spread to become generalized. The attacks were often preceded by a peculiar sensation in the epigastrium and a feeling of constriction in the throat, with pain in the abdomen. The pain might last for several hours, or for 2 or 3 days. Frequently, the premonitory symptoms occurred without being followed by convulsions. The neurologic examination revealed a hyperactive knee jerk on the left side, horizontal nystagmoid jerks on looking to either side and a left homonymous defect in the visual fields. An encephalogram made on June 27, 1934, was interpreted as showing subcortical atrophy of the right hemisphere.

An accurate account of the convulsions before she came under observation was difficult to obtain. She was known to have been on phenobarbital, but the details of treatment were not known. It was necessary to enlist the help of her family to get her to come to the clinic regularly and to obtain an accurate report of her attacks.

Histamine hydrochloride 0.5 cc. of a 1 to 1,000 solution was given intramuscularly at weekly intervals from July, 1934, to January, 1935. During this 6-months period major convulsions occurred once or twice a month. The patient might go a week without the feeling of constriction in the throat and then the sensation would recur daily for several days. It might last a few hours, or might last the greater part of a day. It was her impression that by drinking water this sensation sometimes could be avoided, and she thought that if she failed to drink water a major convulsive attack would follow.

In January, 1935, the patient was put on Bellergal, 1 tablet 3 times a day. The dosage was increased to 4 tablets a day in February. From January to February, 1935, she was given 3 tablets a day; from February, 1935, to January, 1936, 4 tablets a day; and from January, 1936, until June, 1936, 3 tablets a day. From January, 1935, to June, 1936, when these data were collected, the patient had had no convulsive attacks, but at irregular intervals she continued to have minor attacks consisting of the peculiar sensation in her throat.

Case 2: E. H., a white female, aged 40 years, began to have "dizzy spells" at the age of 36 years. The onset of the convulsive seizures occurred at the age of 37 years. The frequency of attacks was 1 every 6 to 7 weeks, with periods of 24 to 48 hours during which time she would have 6 or 7 attacks. The convulsions themselves were typical grand mal seizures. An encephalogram had been made at the Temple University Hospital in June, 1933. There had been no change in the number or the severity of the attacks following this time.

Physical examination revealed hypertrichosis, soft systolic apical murmur, and bilateral prominence of both eyes. Neurological examination revealed diminution of vibration sense in the lower limbs, questionable weakness in the right hand, and absent abdominal reflexes. The blood Wassermann was negative; the visual fields and eyegrounds were normal; an X-ray film of the skull was negative. An encephalogram made on December 11, 1934, was negative. The examination of the cerebrospinal fluid showed 41 mg. per cent protein, 7 cells per cc., a negative Wassermann test and a colloidal gold curve of 0001222100.

The patient was put on Bellergal tablets, 4 a day, before discharge from the hospital in December, 1934. She had no attacks until August 24, 1935, at which time she had a series of grand mal seizures. She was then given Bellergal, 1 tablet 4 times a day reinforced with small amounts of phenobarbital, ½ grain once daily, at 11 A. M. The patient went until January 24, 1936, without any attacks, when she had 4 or 5 attacks while sleeping. She had another attack on March 7, 1936, while at a movie where she was frightened by the picture of a rat. She is now on Bellergal, 6 tablets daily.

Case 3: S. R., a white female, aged 36 years, had had her first convulsive seizure at the age of 30 years. The attacks were generalized. From 1930 until 1934 she had only 5 convulsions. During the summer of 1934 the attacks began to occur about once every 2 or 3 weeks.

The physical examination disclosed the signs of mitral stenosis. The neurological examination showed the pupillary reaction to be sluggish and the abdominal reflexes diminished or absent. An encephalogram made on November 6, 1934, showed enlargement of the left lateral ventricle. A suggestion was made that the enlargement of this ventricle might be due to atrophy of the brain or some other developmental anomaly. The encephalogram had no effect upon the severity or number of attacks.

She was continued on phenobarbital, and in the 3 months following discharge she had 4 convulsive seizures. On January 30, 1935, the patient was put on Bellergal, 1 tablet 4 times a day, and on February 27, 1935, this was increased to 6 times a day. Two weeks later the amount was decreased to 5 times a day, which dosage has been continued ever since. The patient was absolutely free of attacks during the summer of 1935. She stopped taking Bellergal for 4 days during which time she took 3 grains of phenobarbital daily. The phenobarbital, however, made her very weak and tired, and she again took Bellergal. She has been entirely free of seizures for a period of over 1½ years on this medication.

Case 4: C. W., a white female, aged 9 years, began to have convulsions at the age of 8 years. The attacks were definitely limited to the left side of the body including the upper and lower extremities. The first attack was very severe and necessitated the use of chloroform to stop the convulsive movements. In November, 1933, and on December 8 and 11 of the same year the patient had similar attacks. While in the hospital in January, 1934, she had 3 convulsions. She was discharged February, 1934, and 2 weeks later she had another convulsion involving the same areas and requiring chloroform to stop the attack. Other than these she had experienced 2 less severe attacks lasting a shorter time.

The physical examination showed adenoid facies, poor body development, nystagmus on looking to the extreme left, muscular atrophy of the left leg, palpable liver and kidneys, systolic cardiac murmur, possible atrophy of the small muscles of the left hand. The neurological examination showed possible dysdiadokokinesia of the left hand, and slightly hyperactive knee and ankle jerks on the left. A roentgenogram of the skull was negative. The visual fields showed contraction, chiefly bitemporal. On April 12, 1934, an encephalogram was made which showed a right frontal porencephalic cyst.

The patient was put on phenobarbital, ½ grain twice a day, and discharged from the hospital. In July, 1934, she had 2 slight attacks localized to the left side of the body and lasting 5 minutes each. She was then free of attacks until October, 1934, when she had convulsions limited to the left side. She had 2 convulsions in October and 2 in November, each lasting 10 minutes and confined to the left arm and leg. These were preceded by a feeling of pins and needles and were followed by partial paralysis of the limbs. She was continued on phenobarbital in the same dosage. She was free of attacks until January, 1935, when she had another attack lasting a short time. In the first 2 weeks of February she had 3 attacks all limited to the left side of the body and lasting only a short while. She was put on Bellergal, 4 tablets daily on February 27, 1935. She then had no attacks until July, 1935, at which time she had 2 mild attacks involving the left arm and leg. She continued on Bellergal up until June, 1936, during which time she had no attacks.

DISCUSSION

Obviously, this is not a study of the comparative value of dehydration, phenobarbital, bromides, or drugs having their chief action upon the autonomic nervous system. It is, however, an effort to evaluate whether or not phenobarbital combined with ergotamine tartrate and bellafolin is of value in cases refractory to phenobarbital alone. As shown in the table, only 4 patients (19 per cent) showed great improvement with Bellergal, but an additional 9 (43 per cent) showed either a diminution in the frequency of attacks or an improvement in their character. In the group of those slightly or moderately improved were several patients in whom the frequency of attacks was reduced by 50 per cent.

This improvement seemed to make an inquiry into the mode of action of Bellergal worth while. While the effectiveness of phenobarbital in generous doses in the symptomatic treatment of epilepsy is indisputable, nevertheless, in our opinion, the amount of this drug contained in Bellergal does not entirely account for the beneficial results secured with it. As for ergotamine tartrate, Karlsberg used this drug successfully in 2 patients for the prevention of epileptic attacks that were associated with the catamenia. The bellafolin component has been shown by Meggendorfer and others, to intensify the action of phenobarbital in a manner that is especially valuable in the prevention and control of epileptic attacks. Some additional light may be thrown upon its mode of action, however, from its use in other clinical conditions and in the experimental laboratory. Perhaps the direct pharmacologic effect of Bellergal upon epileptic manifestations may even be less important than its general sedative action upon the entire nervous system. Bickel stated that in all paroxysmal diseases the best treatment of these conditions consisted in modifying or correcting the neuropathic terrain upon which they developed.

According to Rothlin, ergotamine paralyzed both the motor and inhibitory endings of the sympathetic nervous system. It bears the same relation to the sympathetic division of the autonomic nervous system that atropine bears to the parasympathetic. Ergotamine tartrate has been used for a number of years for the symptomatic treatment of migraine. Abrupt termination of the initial attack of migraine treated with ergotamine tartrate by Lennox occurred in 40 or 45 cases. Merwarth and Freimann agreed with Lennox and said "the classical migraine attack can be helped in most instances with ergotamine and no remedy hitherto proposed has had the uniform success in relieving the pain." In an attempt to find the reason for these beneficial results, Lennox, Gibbs and Gibbs found that this drug caused a moderately increased flow of blood through the brain. This effect, however, they thought was secondary to an increase of the systemic blood pressure; and in their opinion, it does not explain the relief of headache which follows its injection. In discussing the action of ergotamine, Lennox said: "If one assumes that vascular spasm is the cause of migraine, ergotamine tartrate, while paralyzing the motor sympathetic, may relieve the spasm and the pain. On the other hand, one might assume that small doses of ergotamine act on sensory nerves with elimination of painful stimuli without necessarily altering the caliber of vessels and the cerebral blood flow. In this connection, the relief of pruritus by ergotamine tartrate is suggestive. The time interval between injection and relief is the same for both pruritus and headache. As yet unexplained is the fact that after subcutaneous injection, blood vessel changes and uterine contractions begin almost at once, but clinically, relief of headache following the administration of ergotamine does not begin for nearly an hour." By way of illustration, this author mentioned one patient who had complete bilateral sympathectomy without influence upon the headache, but in whom ergotamine tartrate subsequently aborted each attack. Whether this is therapeutic evidence against the exclusive importance of the sympathetic nervous system, as Lennox said, is not certain, because it is extremely difficult to know when all the sympathetic fibers have been completely interrupted. Relief of migrainous headache was also obtained by the use of this medicament by Brock, O'Sullivan and Young, yet other measures supposed to induce vasodilatation of the cerebral blood vessels did not give invariable relief. These authors found that acetylcholine gave striking relief in a few cases unaffected by ergotamine tartrate, but that histamine was not only of no benefit in their series but was quite apt to intensify or provoke the pain. In further support of the localization of the effect of ergotamine upon the blood vessels, Frommel noted that this drug increased the tonicity of smooth muscles, particularly those of the arterial walls, and thus kept in check the abrupt changes in this tonicity during minor excitation of the sympathetic.

Not only does ergotamine tartrate relieve migrainous headache and pruritus in many instances, but it is also known to produce an alteration in behavior. Rothlin found that ergotamine administered to guinea-pigs, rabbits and cats appeared to have a quieting effect upon these animals. In a continuation of his experimentation, he gave phenobarbital in doses sufficient to produce quietness or mild motor impairment, such as weakness or slight ataxia, and then as a result of combining a similar dose of phenobarbital with ergotamine he obtained definitely more intensive effects than resulted from phenobarbital alone. Hess has reported that the intraventricular injection of ergotamine diminished psychic activity in cats so that the animals became somnolent, disinterested in chasing mice and in other ways exhibited an inhibition of psychic activity without narcosis. Cocaine, on the other hand, increased the psychic activity of his animals. A favorable influence of ergotamine tartrate upon the behavior of psychotic patients has been reported by Baber and Tietz. Their thesis is that by suppressing the activity of the sympathetic nerves ergotamine might suppress those abnormal behavior activities which seem to be associated with sympathetic over-excitation. Small doses administered orally to a series of 62 patients who had previously failed to respond to the usual treatment, such as hydrotherapy, occupational therapy, and the more commonly used drugs, tended to diminish suicidal, homicidal and destructive activity. The patients ate better and frequently became more tidy in their toilet habits. The greatest successes occurred in the manic-depressive groups.

Whether the bellafolin contained in Bellergal contributes to its beneficial effects is not known. In his animals, Rothlin saw no manifest change in their conduct when bellafolin was given. Simultaneous medication of bellafolin and ergotamine tartrate caused mild but manifest quietness. He concluded from his experiments that by combining bellafolin, a vagus inhibitor, with ergotamine, a sympathetic depressant, no change in the effect of either occurs, but that both drugs act specifically upon different portions of the autonomic system. Whether the bellafolin contained in Bellergal is of value or whether the phenobarbital and ergotamine tartrate of this product minus the bellafolin would be equally as efficacious is not known. We are not aware of any evidence that bellafolin is beneficial in the convulsive state, yet the question is raised by the work of Cushing, who demonstrated that the injection of pituitrin into the ventricles in man produces an effect opposite to that caused by the subcutaneous or intravenous injection of pituitrin. It causes profuse sweating, nausea, vomiting, fall in body temperature, fall in metabolism—essentially parasympathetic stimulation. Pilocarpine injected into the ventricles causes a similar effect. The nausea, vomiting and other symptoms can be stopped by the administration of atropine into the ventricles or subcutaneously. Atropine administered prior to the injection of pituitrin or pilocarpine into the ventricles prevents the appearance of sweating, nausea, vomiting, etc. Thus a series of parasympathetic phenomena apparently aroused by central stimulation can be stopped or prevented by atropine. Whether the nausea and vomiting associated with some convulsive attacks can likewise be prevented by atropine is not known, but if these unpleasant symptoms are the result of parasympathetic erethism, medication with an active belladonna product is quite likely to prove effective.

While the detailed pharmacologic effects of Bellergal may not be entirely clear, nevertheless, our experience suggests that its wide-spread sedative action upon the neurovegetative system renders it a valuable therapeutic agent in certain cases of epilepsy. That there is a clinical basis in epilepsy for the use of sedatives of the autonomic nervous system in combination with phenobarbital has been recently emphasized by Yakovlev. In an excellent discussion and analysis of epileptic seizures, he stated that "during the phase of the epileptic seizure proper the sympathetic or posterior hypothalamic mechanism (mammillary body and posterior wall of the third ventricle) is overstimulated, while the parasympathetic or anterior hypothalamic mechanism (tuber cinereum and rostral wall of the third ventricle) is inhibited, this relation being eventually reversed during the phase of recovery." It is in the hope of sedating this portion of the nervous system that Bellergal and preparations like it may be effective. Because of the small number of cases in our series and the short duration of their treatment, both of which are hazardous for drawing definite conclusions in so spontaneously fluctuating a syndrome as epilepsy, our work has only been suggestive and merely points the way to further study of the effect of combined autonomic and central nervous system sedation in the convulsive disorders.

Summary and Conclusions

In a group of 21 patients with convulsive attacks in whom the usual methods of treatment had failed, the combination of phenobarbital, ergotamine tartrate and bellafolin caused great improvement in 19 per cent and slight or moderate improvement in an additional 43 per cent. It is unlikely that the phenobarbital content of the preparation alone accounted for the beneficial results. The evidence suggests that both bellafolin and ergotamine tartrate supplement and reinforce the action of phenobarbital, and this combination of drugs seems to have a place in the treatment of epileptics who prove refractive to the routine methods of treatment.

Comparative Results Obtained with the Various Medicaments Used

MEDICATION	GREAT IMPROVEMENT	SLIGHT OR MODERATE IMPROVEMENT	NO IMPROVEMENT
Bellergal*	4	9	7
Histamine	0	2	4
Ephedrine	0	1	2
Acetylcholine	0	0	2

* Bellergal—each tablet contains 0.0001 Gm. bellafolin (brand of levorotatory alkaloids of belladonna leaves), 0.0003 Gm. gynergen (brand of ergotamine tartrate) and 0.02 Gm. phenobarbital.

The Bellergal used in these patients was supplied by the Sandoz Chemical Works of New York City.

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METHODS OF DIAGNOSIS OF FEMALE ENDOCRINOPATHIES*

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Time was when only freaks—giants, dwarfs and imbeciles—were referred to endocrine study. Most cases recognized as such were hopeless so far as any beneficial therapy was concerned and little attention was paid to them except as curiosities. But, as the science of this branch of medicine has developed in the past 20 years, we have reached a state where many mild functional conditions have been proven to be endocrine in origin; and we now have effective methods of treatment. So it behooves us all to know how to make a diagnosis of an endocrine disturbance. This cannot be done by a single laboratory test or partial physical examination, but can be arrived at only by following a definite routine of careful study to glean many small facts which when analyzed and correlated become more significant and usually assume the form of a definite clinical entity.

GENERAL SURVEY

The first step in this study occurs when the patient enters the consultation room, in what we may call a general "sizing-up." With what type of person, physically and mentally, have we to deal? Is she either obese or underweight, tall or short? How does she carry herself? Is she mentally alert, cheerful, sluggish, depressed or emotionally unstable? These and many other impressions can be gained in the first few minutes of the interview, and checked and elaborated upon as the study is pursued. They offer valuable aid in making the final diagnosis.

HISTORY

It is needless to say that a careful and complete history must be taken. We shall not go into the minutiae of a history, but certain aspects are sufficiently important to warrant special consideration.

Chief Complaint. In an endocrine history, this may be of little importance. More often than not it will be some vague complaint, such as nervousness or fatigue. The real complaint or complaints are revealed as the history develops.

History of Present Illness. To what time of life is the onset dated? Very often endocrine disturbances first become evident during or after some period of particular physical stress or strain, such as adolescence, pregnancy or menopause. Acute infections are especially prone to depress endocrine function. An operation may have been the precipitating factor, either removal of an endocrine gland (which is all too often the case, especially in women) or as a result of the anesthesia, shock, etc.

The chronological development of symptoms and their association with events may be quite significant.

Menstrual History. The menstrual history is exceedingly important, not only as indicative of ovarian function, but also of practically every other endocrine gland. Disturbances of the thyroid, pituitary and adrenals result in menstrual abnormalities which are fairly typical. The age of the onset of the cycle should be determined; occurrence before 10 and after 16 years of age indicates some disturbance of the normal function. Is the period regular as to occurrence, duration and amount? Has there been any change in the character of the cycle since its onset, that is, does the period occur more or less often; is it more or less profuse; are pain, blood clots, headache, nausea, acne, mental depression, enlarged and painful breasts accompanying features?

What is the fertility of the patient? How many pregnancies have occurred; also, have there been spontaneous or induced abortions? Habitual abortion may be a very definite endocrine stigma. Have contraceptives been used, and if so, what? We know that simple douches are usually ineffective for a normal pair of individuals. If the patient has relied upon douches alone which have apparently been effective, we may be justifiably suspicious that a low degree of fertility is present in one of the partners. It may be due to incompetence on the part of the male, organic pathology probably as result of infection in either partner, or anovulatory menstruation.

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* Presented at the Postgraduate Clinic of the George Washington University School of Medicine, February, 1937.

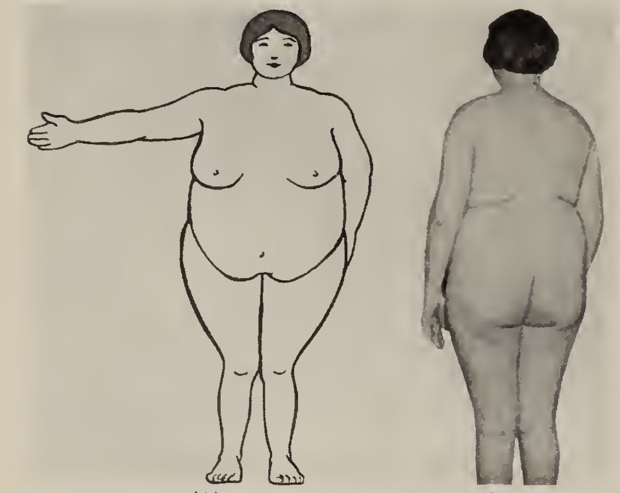
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Fig. 1. Pituitary Obesity. (A) Diagrammatic drawing showing the typical location of the obesity which is limited to the trunk while the extremities are often small and delicate. (B) Case. Female, aged 32 years, height 65 inches, weight 207 pounds, oligomenorrhea.

Fatigue. Fatigability and asthenia, unrelated to activity, are very common findings in all types of endocrine disorders. Although it is unwise to try to delimit the types too sharply, the various endocrine clinical entities have differences which are suggestive. The hypopituitary patients have less endurance. They may be able to carry on but at a much greater expense of energy than is normal and with lessened effectiveness. The hypothyroid individual wakes up tired in the morning, but as the day progresses begins to feel stronger and more energetic until a peak is reached after which there is a slump back to the exhaustion of early morning. The patient with ovarian dysfunction is tired all the time. In the adrenal cases in the early stages asthenic crises occur, periods of real exhaustion developing very rapidly after periods of comparative well being; in more advanced cases the asthenia becomes continuous.

Past History. The past history should include besides the usual data the growth history of the patient, that is, size at birth and the curve of increment of height and weight, the time of teething, walking and talking. A record of progress in school gives an indication of mental growth of the individual.

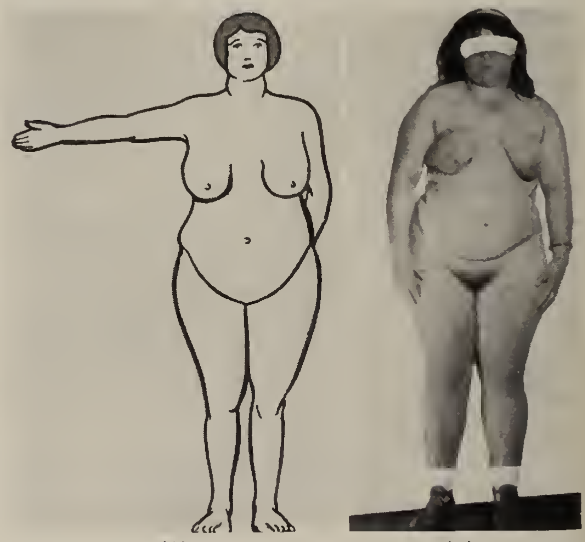
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Fig. 2. Adiposogenitalis (Frolich's Syndrome). (A) Diagrammatic drawing showing the typical location of the obesity which is generalized but more pronounced in the mons, mammary and girdle regions and which is associated with hypogonadal development. (B) Case. Female, aged 14 years, height 64 inches, weight 164 pounds, trunk obesity with poor genital development and amenorrhea.

Family History. Besides the usual facts, one should elicit whether there is any kind of endocrinopathy in the family, not only the one of which the patient complains, but any others.

After a careful history is obtained, it should be reviewed and any suggestive data should be enlarged upon as much as possible. A history so taken will serve as the foundation for further study and will constitute about 50 per cent of the basis for diagnosis.

Physical Examination

As with the history, a complete examination should be made, but certain phases are more apt to give endocrine information than others.

Anthropometry. Anthropometric studies are important. The height has more significance when it is divided into the upper and lower measurements and compared with the span. In a normal adult the upper measurement is equal to or slightly greater than the lower and the span is about equal to the height. In hypogonad and eunuchoid persons the lower measurement is considerably greater than the upper measurement and the span is increased; whereas, in primary hypopituitary persons the infantile type is maintained with shorter lower measurements and span. The actual height as compared to normal gives an insight into the growth mechanism of the body. The height a person is to attain by maturity depends upon the growth impulse plus the time of closure of the epiphysis. Many of the endocrine glands enter into the maintenance of this balance.

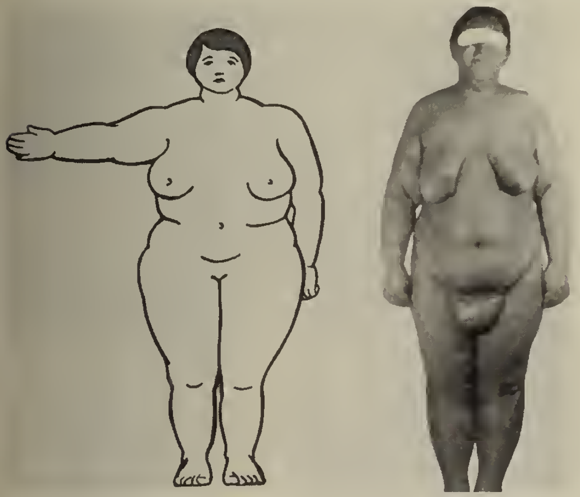
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Fig. 3. Hypothyroid Obesity. (A) Diagrammatic drawing showing generalized obesity with padding of the dorsum of the hands and feet and in the supraclavicular region. (B) Case. Female, aged 27 years, height 63 inches, weight 174 pounds, skin dry and coarse with non-pitting edema, hair coarse and scanty.

Weight varies also with endocrine disturbance. Undernourishment occurs in eunuchoid, hyperthyroid, hypoadrenal individuals, while obesity may be of thyroid, pituitary or ovarian origin. In obese patients the distribution of fat should be determined. The typical pituitary obesity (Figs. 1 and 2) is one in which most of the fat is around the shoulders and abdomen, the so-called girdle obesity; large aprons of fat are often found. The extremities below elbows and knees are usually small and well-formed. In obesity due to hypothyroidism the fat is more generally distributed, with pads in the supraclavicular regions, back of the neck, and dorsum of the hands and feet (Fig. 3). Occasionally non-pitting edema is found. In hypogonadal obesity trochanteric pads are characteristic; often thick, heavy, unshapely legs are pinned to a small body (Fig. 4). In the extreme cases, this typical distribution may be obscured (Fig. 5).

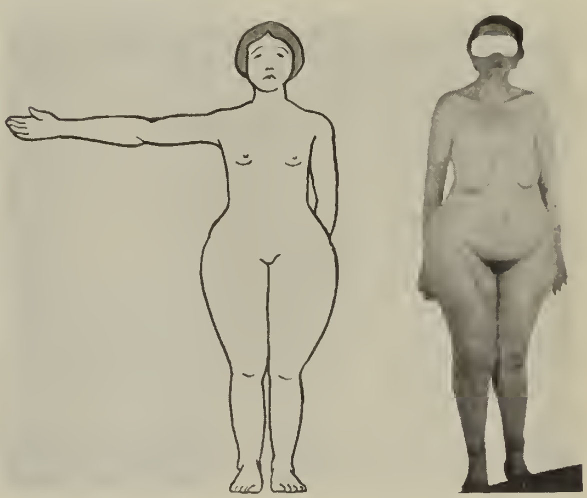
(A) (B)

Fig. 4. Hypogonadal Obesity. (A) Diagrammatic drawing showing the typical location of the obesity which is limited to the lower half of the body with accentuation in the trochanteric region. (B) Case. Female, aged 32 years, height 64 inches, weight 164 pounds, scanty fine hair, small breasts, oligomenorrhea.

Distribution of Hair. In considering the hirsute adornment of an individual as a diagnostic aid, the amount and distribution must be considered in relation to sex and age. Due consideration must be given to such factors as race and occupation in establishing the criterion for normal. Scanty amount of hair is present in both hypopituitary and hypothyroid cases in which the underactivity was initially associated with the early years of growth and development. Hypertrichosis is more often associated with ovarian failure, adrenal tumor or pituitary disturbance. More important than amount is the reversion to the male type of distribution; masculinization of the female suggests ovarian, adrenal or pituitary disease. While none of these findings are pathognomonic, they certainly carry implications of endocrine involvement. The growth and texture of the hair should also be considered (Figs. 6 and 7).

Skin. The skin should be examined for texture, eruptions, and pigmentation. Coarse, dry skin is suggestive of thyroid deficiency, while extremely soft thin skin is found in pituitary and ovarian deficiency cases. Eruptions, particularly acne, are often associated with ovarian disturbances. Pigmentation is more characteristic of adrenal disease but does occur in ovarian dysfunction and in association with diabetes. The purplish striae are often associated with one type of pituitary disturbance.

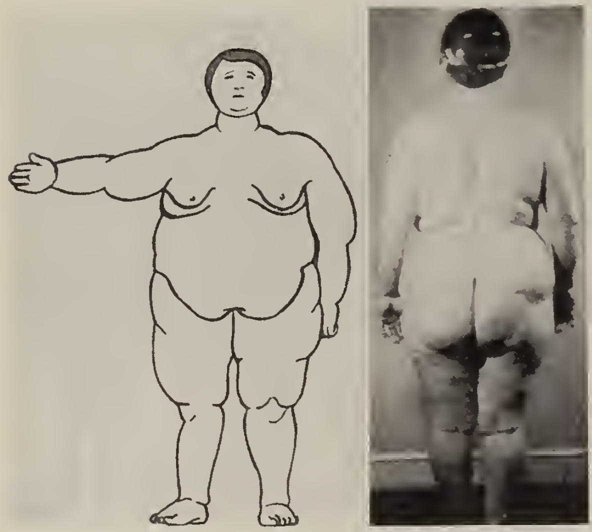
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Fig. 5. Dercum's Disease. (A) Diagrammatic drawing showing the generalized obesity of pituitary type associated with nodules of fat which are painful. (B) Case. Female, aged 46 years, height 65 inches, weight 275 pounds, marked generalized obesity with tender nodules of fat, menopause.

Eyes. Eye examinations yield valuable endocrine information. The eye signs of hyperthyroidism are familiar to all. Besides external examination, peripheral fields, visual acuity and fundus examinations should be made.

Teeth. Teeth should be examined for general formation and growth. Disturbance in the growth mechanism is reflected in dental eruption, placement, size, form and calcification. Some of the characteristic dental defects are the delayed eruptions in hypothyroidism with its concomitant malpositions and malalignment. In hypopituitarism of the anterior lobe miniature teeth are seen; whereas, in the hyperactive state, separation of large densely calcified teeth occur. In hypogonad cases relatively small or congenitally absent lateral incisors are found.

Breasts The development of the breast is one of the secondary sexual characteristics and as such is indicative of the state of activity of the glands concerned with this function. In pituitary infantilism and hypogonadism the breasts are small and poorly developed. In pituitary obesity the mammae constitute one of the sites of predilection for the accumulation of fat. In hyperfunction of the gonads there is excessive development of the breasts (Fig. 8).

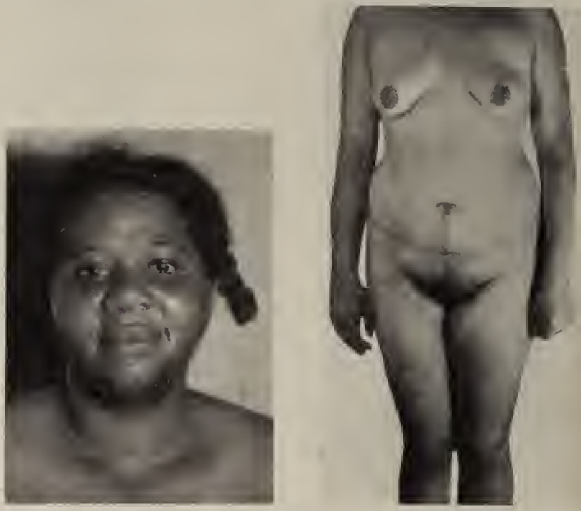
(A) (B)

Fig. 6. (A) and (B). Hirsutism in the Female.

External Genitalia. What has been said of mammary development applies to the external genitalia. Hyperfunction of the pituitary, gonads or adrenals may be evidenced by precocious development in young or excessive development in mature individuals. Reversion to male type with male distribution of hair and enlarged clitoris are suggestive of tumor of the adrenal or arrhenoblastoma of the ovary. Infantilism bespeaks hypofunction of the pituitary or ovary.

LABORATORY EXAMINATIONS

Laboratory examinations form an integral part of any endocrine survey as they do in any other study, but they should not be ordered indiscriminately with the expectation of finding the clinical diagnosis in the laboratory report.

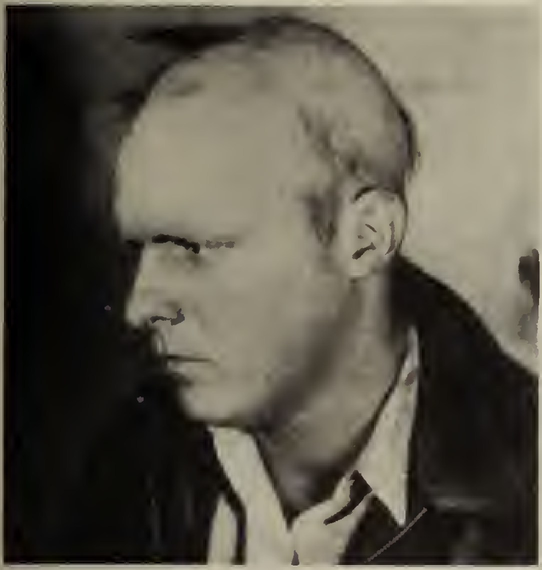

FIG. 7. Loss of hair, probably of endocrinal origin.

Urinalysis. Twenty-four-hour urinalysis should be done on all patients, more to exclude other diseases than with expectation of finding informatory evidence of endocrinopathies. Positive laboratory findings should not be interpreted as renal in origin in all cases. Endocrinopathies do produce such changes as albuminuria, etc. The urinary findings in diabetes mellitus and diabetes insipidus are familiar to all.

Blood Picture. A complete blood count should be done in all cases. Anemia is a common finding in functional menstrual disorders, whereas a high hemoglobin and erythrocyte count are often found in hypopituitary cases. Hyperthyroidism is often accompanied by lymphocytosis. Leukopenia is a common finding in many of the endocrinopathies and may account to a large degree for the low resistance and high susceptibility to infection.

Basal Metabolic Rate. Blood pressure, pulse and temperature are significant indications of the state of metabolism of the body and should be recorded.

Basal metabolic rates should probably be included in all routine studies, but it should be remembered that the test is subject to many errors, and weight should be given only to results which corroborate other clinical data. It is well to determine the blood pressure and pulse rate at the same time as the basal metabolism test is taken, first to be sure that as nearly basal conditions as possible have been attained for the test and serve as a check for the basal metabolic rate itself, using the formula—pulse pressure plus pulse minus 110 equals basal metabolic rate.

In adults, blood cholesterol determinations are probably more significant than the basal metabolic rate; whereas, in children, X-ray study of the epiphyses will probably give better information as to thyroid function.

Blood Chemistry. Quantitative changes in the chemical elements of the blood occur in many types of endocrinopathies. The substances the metabolism of which are controlled directly by specific endocrine glands are naturally the ones which show greater variations and have a more specific significance. In this group are found sugar, cholesterol, calcium and phosphorus.

Glucose Tolerance Test. A glucose tolerance test is the procedure of choice in studying carbohydrate metabolism. Its use should not be limited to cases of suspected diabetes mellitus but should be included in the study of all suspected endocrinopathies. An increased sugar tolerance curve, demonstrated by failure of the blood sugar to rise after the ingestion of glucose to the normal amount (150 maximum) is found particularly in hypopituitary cases, but also in hypothyroidism, Addison's disease and hyperinsulinism; whereas, a decreased sugar tolerance, demonstrated by an excessive rise, is found notably in diabetes mellitus but also in hyperthyroidism and hyperpituitarism.

Blood Cholesterol. The function of cholesterol in the body is unknown. The significance of its chemical relationship to the sex hormones and vitamins A and D is a very intriguing problem. We do know, however, that there is an excessive amount present in the blood in diabetes mellitus and hypothyroidism, findings which especially in the case of the latter offer exceedingly important confirmatory evidence of hypofunction.

Blood Calcium and Phosphorus. Calcium and phosphorus are mainly important in the study of parathyroid disturbance.

Hormone Tests. By biologic assay we can now determine with a fair degree of accuracy the blood and urine levels of the sex hormones, the estrogenic and gonadotropic substances. The use of these tests offers material aid in ascertaining the degree of ovarian and pituitary function in the functional disorders of the female.

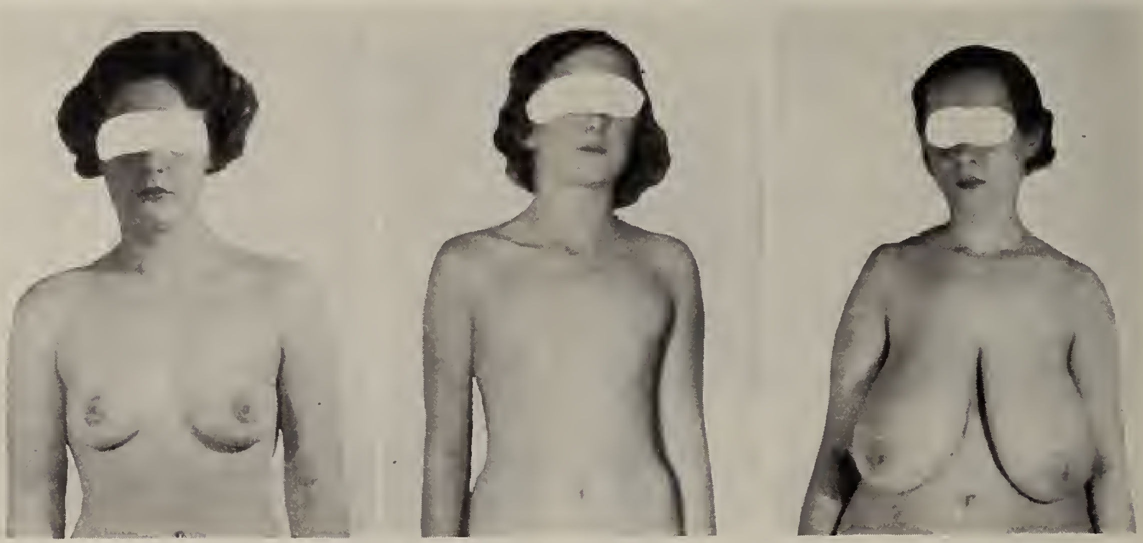
(A) (B) (C)

Fig. 8. Development of Breasts. (A) Normal. (B) Underdevelopment in female aged 27 years. (C) Excessive development in female aged 24 years.

Since the female sex hormone, theelin, is produced in a cyclic manner, repeated tests over a period of a month give more complete data than a single test. This, however, offers practical difficulties and in cases in which it is impossible to make repeated tests, one test taken just prior to the onset of menstruation may be helpful. The theelin level is decreased in some cases of amenorrhea, oligomenorrhea and late menopause. It is increased in functional bleeding, dysmenorrhea and early menopause.

The pituitary gonadotropic element is not demonstrable in normal cases except occasionally at the time of ovulation. It is increased in cases of functional disorders resulting from primary ovarian failure, as amenorrhea or menopause. Thus we are able to differentiate primary ovarian and primary pituitary failure. The hormone is also increased in pregnancy, in which it constitutes the basis of the Aschheim-Zondek and Friedman tests for pregnancy.

Uterine Scrapings. Studies of the endometrium at varying stages of the cycle offer perhaps the best method of diagnosis of ovarian function which we have available today. From such studies we are able to ascertain the effectiveness of both ovarian hormones, theelin and progestin, upon the growth of the endometrium. We are able to say whether or not ovulation has taken place, a very important finding in studies of cases of sterility.

X-ray Examinations. X-ray examination is used to give direct evidence as to the appearance of the ossification centers and the closure of the epiphyseal junction. There is a delay of closure in pituitary infantilism, pituitary giantism, hypogonadism and hypothyroidism. Hypergonadism accelerates epiphyseal closure. X-ray of the sella turcica in all pituitary cases is advisable in order to determine any enlargement or diminution in size, erosion, or bridging of the clinoids. Parathyroid disease is evidenced by alteration in structure of bone.

Typical laboratory findings in endocrinopathies are summarized in the accompanying chart.

In conclusion, a positive diagnosis of endocrinopathy should be made only after all non-endocrine causes for the disturbance under consideration have been satisfactorily ruled out. In the study of many cases endocrine conditions may be discovered which must assume a secondary position so far as the treatment and prognosis of the case are concerned, since a non-endocrine factor may be of greater importance. The reverse is also true. Hence, the diagnosis of endocrinopathies can and should be made only after a careful complete study of the individual as a whole.

Significant Positive Laboratory Findings in the Endocrinopathies

TEST	RESULTS		
	Normal	Increased	Decreased
Urinalysis:			
Amount	1200–1500 cc. per 24 hours	Diabetes insipidus Diabetes mellitus	
Specific Gravity	1.008–1.030	Diabetes mellitus	Diabetes insipidus
Sugar	None	Diabetes mellitus Hyperthyroid	
Basal Metabolic Rate	Minus 10 to plus 10	Hyperthyroidism Hyperpituitarism	Hypothroidism Hypopituitarism Addison's Disease
Blood Chemistry:			
Sugar tolerance	Maximum, 150 mg. per 100 cc. with return to normal in 2 hours	Hypopituitarism Hypothyroidism Hyperinsulinism Addison's Disease	Hyperpituitarism Hyperthyroidism Diabetes mellitus
Cholesterol	150–190 mg. per 100 cc.	Hypothyroidism Diabetes mellitus	Hyperthyroidism
Calcium	9–11 mg. per 100 cc.	Hyperparathyroidism Hypothyroidism Hyperpituitarism	Hypoparathyroidism Hyperthyroidism
Phosphorus	3–5 mg. per 100 cc.	Hypoparathyroidism	Hyperparathyroidism

A NEW TYPE OF TREPHINE BURR FOR SIMPLIFYING NEUROSURGICAL TECHNIC

John J. Shugrue, M.D.

Professor of Neurosurgery, Georgetown University School of Medicine

The object of this paper is to present a preliminary report of an especially devised type of skull (bone) burr, adjustable as to depth, and the uses to which it may be applied. Rather than give a technical description of the burrs, the reader is directed to a study of the illustrations, to note especially the type of bit used and its contact point (Figs. 1 and 2). The larger bit is the hardest type of steel spiral drill in ordinary commercial use, except that the contact point is relatively flattened.

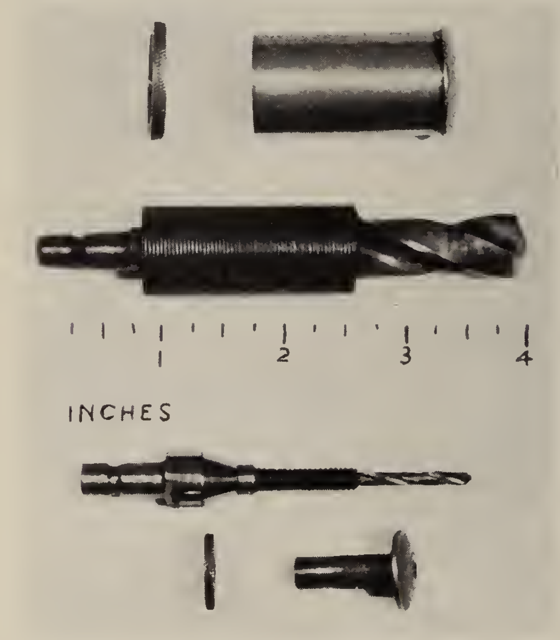

Fig. 1. Larger and smaller burrs unassembled.

The larger burr consists of three elements: the screw-threaded body portion, the sleeve and the lock-nut. The screw-threaded body portion consists of the bit, the threaded portion and the shank, all in one solid piece. The sleeve is threaded upon the screw-threaded body portion of the drill and may be adjusted so as to regulate the length of the drill and the depth of the boring; the lower end of the sleeve, as shown, is smooth and convex where it contacts the skull in limiting the depth of the drill. The lock-nut threaded to the upper portion of the body prevents sliding of the sleeve. The shank of these drills is made to fit the ordinary trephine socket.

The second smaller burr embodies the same idea attached to the Adson spiral burr. The gage of the burr can be of greater or lesser diameter, depending on the wishes of the surgeon.

The idea of skull burrs adjustable as to depth is not new, but the type of bit described (steel spiral drill with relatively flattened contact point) with the modification lends itself more readily than other burrs to more wide-spread use in skull operations. The larger burr is used in place of the ordinary burrs, such as the Doyen, Hudson, etc., to bore the usual holes in the skull for osteoplastic flaps, etc., (Fig. 3). It has been used and found to be a safe, practical time-saver. In contrast to the above-mentioned burrs or the electrically motor-driven ones, I have found it to have made its holes in half the time and with considerably less energy expended. This single burr replaces the perforator and the enlarging burrs which formerly were considered necessary to make a single hole.

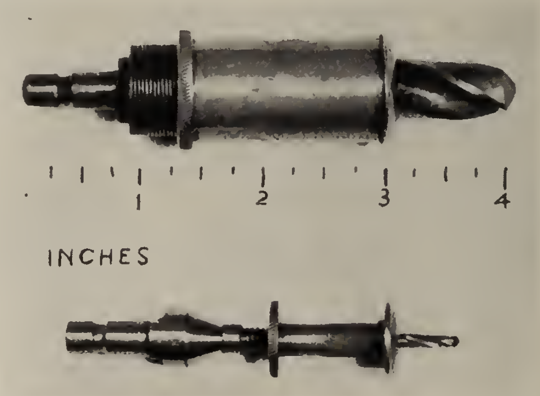

Fig. 2. Larger and smaller burrs assembled.

Should the estimated depth of the burr be greater than the thickness of the skull, after a little experience one finds it automatically locks as it touches the dura and enters the cranial cavity; the harder and thicker the bone the quicker the penetration of this burr. It can be more easily sharpened and retains its keen edge longer than other burrs.

Small holes for tying in the bone flap may be safely made prior to its reflexion. After the larger trephine holes have been cut for a bone flap and either before or after using the gigli saw, small holes can be quickly made, using the original larger burr holes as a guide to depth, thus omitting the delay and trouble in swinging the flap back and forth to place the holes exactly opposite each other. I prefer to make the tie holes after the gigli saw work has been completed.

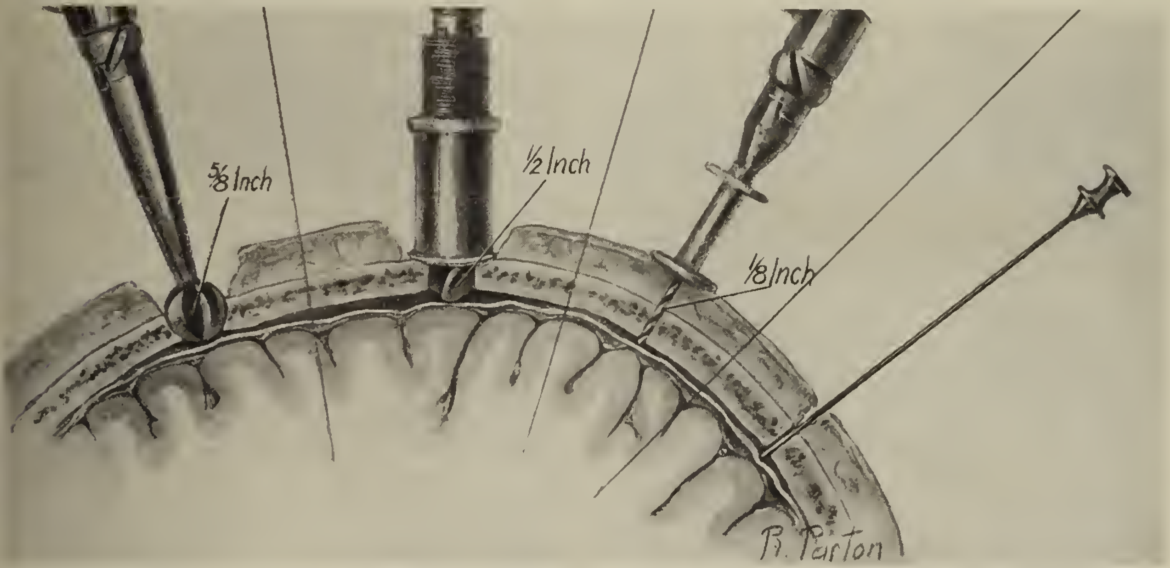

Fig. 3. Diagrammatic drawing showing difference between the old and new burrs in entering the cranial cavity. The burr on left is of the old type. At right a spinal puncture needle is shown entering the cranial cavity through the small trephine opening made by the small burr.

For ventricular punctures for air injection or aspiration a simple puncture wound about the size of the drill to be used (smaller drill of $\frac{1}{8}$ inch diameter) is made in the scalp down to the bone; the smaller drill depth is estimated, usually by the age of the patient and the X-ray thickness of the skull, and the hole in the bone is made down to the dura mater (Fig. 3). There is little or no bleeding; if, however, the skin incision bleeds, a single silk suture will control it. The lumbar puncture needle or the finely pointed ventricular needle is inserted, and the dura and brain are punctured and entered. The advantages of this procedure are as follows: simplicity and speed of method; smaller area of head to be shaved; smaller wound with less bleeding; practically no bother with retractors, hemostats, etc.; and little or no suturing of the wound. The smaller wound allows no herniation of the brain in the trephine wound, less injury to the brain, slow and controlled lowering of the increased intracranial pressure; and finally, when done over the posterior horn of the lateral ventricle, less danger of producing the homonymous hemianopsia that at times follows the usual method of puncture in this area. One may now begin to see the use of the smaller drill for multiple punctures of the head in search of a relatively unlocalized brain abscess. Because of the size of the skin wounds, the vascularity and healing properties of the scalp are unaffected and may be disregarded in large osteoplastic skin incisions. There is less danger of infection in going through these small wounds at a later date. Again, because of the size of the smaller burr holes, there is no danger of carelessly going through them with the knife, periosteal elevator or hemostats, and they may be disregarded so far as the planning of the future bone flap and skin incision are concerned.

For the treatment of spreading osteomyelitis of the skull burr holes are quickly made in front of the advancing infection, all of the same depth, the larger burr being set only to penetrate to the diploe; the periphery of the trephine hole is of the same depth as the center.

To promote the growth of granulation tissue over an area of skull denuded of scalp the advantage of the use of the larger burr is easily seen. Other minor uses are outlining and cutting cosmetic grafts of the skull and small holes for the insertion of screws for steadying purposes in the position of the head, particularly the upright cerebellar or cerebral operation. The burrs may be of value in other branches of surgery.

SUMMARY

A hitherto supposedly dangerous and crude bit (larger drill) has been converted into a fast, useful and safe trephine burr. The smaller drill has simplified certain operative procedures on the skull and brain, and the surgeon can appreciate that in exploratory punctures a larger hole is at times necessary.

Spontaneous Subarachnoid Hemorrhage.—Spontaneous subarachnoid hemorrhage is, as the name implies, the extravasation of blood from rupture of a small vessel into the space between the arachnoid and the pia mater. Frequently unrecognized, once recognized it is rarely missed again. Early recognition and proper treatment save the patient from suffering from permanent injury, even from loss of life. Because of the danger in moving the patient long distances, it is usually imperative that any physician recognize and treat the condition.

There is general agreement that a defect in the vessel wall usually leads to its rupture. Variations in the ramifications of brain arteries around the circle of Willis are described by many. Vivid descriptions of abnormalities of the circle of Willis found at autopsy are given by Bouman.

Blood is found in the subarachnoid space in most serious head traumata. This type of case is not included in discussion of spontaneous hemorrhage. . . .

All of the patients have been treated along the same line. Treatment consists of:

1. Spinal puncture when indicated by following symptoms:
(a) Pulse rate of 60 to 70; rapidly rising b.p.
(b) Violent headache which is not controllable by the usual methods in 24 to 48 hours.
(c) Unconsciousness with or without spactic convulsive seizures.
(d) Continuous vomiting.

If the condition of the patient warrants waiting 24 to 48 hours before doing a spinal puncture, we always prefer doing this. However, any of the symptoms listed under "1" demand immediate spinal puncture, repeated as often as indicated. In order to make a diagnosis, one is justified in doing a spinal puncture provided little fluid is withdrawn. Recurrence of hemorrhage is less likely if we wait 24 to 48 hours to do the spinal puncture.

2. Sedatives—no opiate should ever be given a patient suspected of having subarachnoid hemorrhage. Sodium luminal is indicated in sufficient dosage to keep the patient quiet. One may safely give 5 grains hypodermically and repeat every 2 to 4 hours as necessary.

3. Intake and output of fluid should be recorded. The intake should not exceed 1800 to 2000 cc. for the first 4 to 5 days of illness, and then increased only as indicated.

4. Two cc. of a 25-per cent solution of magnesium sulphate given intramuscularly every 3 to 4 hours, promises good results. Magnesium sulphate by mouth may be used after 3 or 4 days, and hypodermic injections discontinued.

5. In these cases 25- to 50-per cent glucose in doses of 100 to 200 cc. were given intravenously twice daily until definite improvement was present.

Massermann first investigated the effects of intravenous doses of hypertonic solution of sucrose, and found a 50-per cent solution satisfactory for clinical use; and that as high as 500 cc. may be thus given without causing any toxic or other untoward symptoms. Hahn and others make the following statement: "There is considerable advantage in the substitution of sucrose for glucose in the osmotic therapy of increased intracranial pressure occurring in cases of acute brain injury." It is claimed by many authors that the usual preparation of concentrated glucose, or dextrose, immediately following administration, causes a temporary rise in spinal fluid pressure, that this finding is not present following the administration of sucrose solution, and that practically all sucrose given intravenously is eliminated rapidly so there is no danger of accumulative effects following repeated doses. The lack of absorption of sucrose by the body tissues, which can not be said of glucose or dextrose, gives the former preparation a marked advantage as a diuretic, and therefore is much more effective in reducing spinal fluid pressure.

In the cases discussed no sucrose was used. However, in the future I shall employ this preparation in cases of subarachnoid hemorrhage.

Summary.—In all such cases it is important to look for varicose veins; to rule out syphilitic infection; to make a careful study of the blood by means of clotting time, bleeding time, platelet count and tourniquet test. History of injury is important, as is history of chronic alcoholism, arterial hypertension, pernicious anemia and scurvy.

When judiciously treated recovery is the rule. Two of the 10 cases reported were fatal—one due to repeated subarachnoid hemorrhage following violent lifting before healing had taken place; and in the other case hemorrhage must have involved the thermal center and death resulted from loss of control over temperature.

In 4 of these cases no predisposing factor or cause of the hemorrhage was found. Of the other 6, 3 may have resulted from hypertension, while syphilis, varicosities, and chronic alcoholism were factors in the remaining 3.

Abstract from article by P. A. Shelburne, M.D., Greensboro, N. C., Southern Medicine and Surgery, November, 1937, p. 533.

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A SOLUTION

The Society has very wisely gone on record as favoring the postpayment method of enabling the small wage-earner to secure adequate medical care at a price he can pay. By implication this stand emphasizes the attitude of thinking physicians that in the end the public would suffer more than the profession by any form of prepayment or insurance plan. The standard of medical practice by and large would be greatly lowered and medical progress would be retarded. The problem of making the public realize this is a difficult one, since apparently the only champion of this view is the organized medical profession, and that element naturally can easily be accused of self-interest. By far the best way to carry this point is to demonstrate practically the untruth of the contention of proponents of socialized medicine that under the present method of medical practice only the rich and the poor receive adequate medical care. We must prove that every individual in the District of Columbia can receive all necessary medical services irrespective of his economic status.

The first step in this direction is to revivify and to develop to its fullest uses the Medical-Dental Service Bureau, a child of the Society born three years ago after careful study of the shortcomings of medical practice and with full realization that a problem existed. Unfortunately many physicians were too busy and too much "in a rut" to familiarize themselves with the worth and workings of the Bureau. Others claimed they could handle their own business affairs best, not being willing to admit that they did not possess the necessary background nor the time to adequately investigate the socio-economic status of their patients. Still others were unwilling to take their chances of remuneration with other medical servants involved in a case but wanted to "get theirs" first. A small group even begrudged the 10 per cent retention of fees collected for maintaining the Bureau. The Bureau officials have been accused of favoritism, some physicians claiming that their patients were shunted to other physicians. By some the Bureau was looked upon as a collection agency for bad debts, and naturally they were disappointed. Patients were sent to the Bureau who properly should have gone to the Permit Bureau of the Health Department or to the Central Admitting Bureau; and some of the physicians sending them blamed the Medical-Dental Service Bureau because the patient's economic status was found to be such that medical fees could not be paid. All of these things indicate that a certain number of physicians did not understand the function of the Bureau and did not coöperate with it. Consequently it was not utilized to its fullest capacity.

The physician must be broadminded. He must be willing to abide by the decisions of those better qualified to determine the economic status of his patients, and he must be willing to accept less remuneration in all cases in which a careful investigation has revealed the true state of affairs. The Society has now gone on record as agreeing to "play ball" with the Bureau, to utilize it in every justifiable case, and to accept the judgment of the Bureau officials.

It has been proposed to move the Bureau from Eighth and Eye Streets to the Society's building at 1710 M Street in order to make it more readily available to the members, to place it under closer scrutiny, to get it into a better neighborhood, and to separate its clients from less fortunate individuals who are being handled by the Permit Bureau or the Central Admitting Bureau. Naturally the Board of Directors of the Medical-Dental Service Bureau must agree to this move before it can be made. Likewise the District of Columbia Dental Society, the Medico-Chirurgical Society (colored), and the Robert T. Freeman Dental Society (colored) must be consulted, since they are sponsors, spiritual and financial, of the Bureau. It is of the utmost importance that the hospitals coöperate, and it is probable that they will, since their fate is intimately bound up with that of the Society and with the future of medical practice. The hospitals are essential elements in the plan, since an important part of the "high cost of medical care" in many cases is the cost of hospitalization. Also, the clinical laboratories and the X-ray groups must coöperate for the same reason. Experience leads us to believe that they will. Thus the problem involves a coöperative effort of all elements concerned in the care of the sick.

Furthermore, the public must be properly instructed in the principles, advantages and uses of the Bureau. This must be done by proper publicity through the newspapers, by talks before groups of employees and civil organizations, and by the physicians themselves in conversation with their patients. In developing the Bureau, there must, of course, be opportunity for physicians to appeal to an arbitration board and also for disgruntled patients to express any dissatisfaction to a grievance committee. While coercive methods could not be tolerated on the part of the Society toward its members, it is only proper for the Society to expect its members to enter wholeheartedly into the spirit of the plan.

The Society will probably have to house the Bureau in its new quarters without rent, and perhaps for a while the retention fee may have to be raised to 15 per cent until the Bureau makes proper headway. But the time is here when we must demonstrate our willingness to go more than half way to carry our point.

Development of the Medical-Dental Service Bureau to its proper functions alone will not solve all of the problems of medical socio-economics. An unsolved problem is the domiciliary care of the indigent sick. This is properly a function of the state, but the Society can be of great assistance in its solution. However, all reforms cannot be accomplished overnight, and we will probably accomplish more by concentrating on one problem at a time.

TRANSACTIONS OF THE SOCIETY

Stated Meeting, November 3, 1937

The following were duly elected to membership, upon recommendation of the Committee of Censors:

Active Members

Walter Kavanagh Angevine, 6300 Thirteenth Street, N.W.
Edward Ballard Broocks, 1836 Connecticut Avenue, N.W.
Peter Paul Brue, 413 Ingraham Street, N.W.
Ralph Cohen, 1201 Sheridan Street, N.W.
Robert Francis Costello, 2818 Twenty-eighth Street, N.W.
Max Ellis Feldman, 3624 Nichols Avenue, S.E.
Enoch Raymond Fenton, 1835 Eye Street, N.W.
Eugene Antonio Forcione, 200 Massachusetts Avenue, N.W.
Oscar Hugh Fulcher, 1726 Eye Street, N.W.
Aaron Harry Gerber, 2025 Eye Street, N.W.
Reuben Goodman, 1746 K Street, N.W.
John Estes Hanby, 901 Sixteenth Street, N.W.
Alan Frank Kreglow, 1801 Eye Street, N.W.
Charles Edwin McNamara, 1801 Eye Street, N.W.

Associate Member

Thomas Harry Quill, 3700 Massachusetts Avenue, N.W.

Applicants for membership to be voted on in January, 1938:

For Active Membership

Andrew Keene Bowie, George Washington University—1926
Darrell Clayton Crain, Jr., George Washington University—1932
Jules Daniel Damian, Georgetown University—1930
Michael Patrick DeVito, Georgetown University—1932
William Shambough Detwiler, George Washington University—1930
Francis William Dunne, Georgetown University—1929
Otto Anderson Engh, Temple University—1933
Andrew Browne Evans, Georgetown University—1922
Irvin Feldman, George Washington University—1933
Nathan Glaubach, George Washington University—1935
Milton M. Greenberg, George Washington University—1933
Robert Barron Havell, George Washington University—1935
Eugene Witter Higgins, Georgetown University—1936
William Hollister, University of Maryland—1922
William Dabney Jarman, University of Virginia—1932
Elmer Klein, Indiana University—1925
Edward Burke Kelly, Georgetown University—1928
Richard Joseph Kemp, University of Maryland—1921
Sander Edwin Lachman, Johns Hopkins University—1926
Zigmond Meyer Lebensohn, Northwestern University—1934
Thomas Francis Lowe, Georgetown University—1902

John William Mann, University of Pennsylvania—1917
Agnes Louise McNutt, George Washington University—1936
Kemp Hammond Mish, George Washington University—1933
Arthur Nachlas, University of Maryland—1932
John Manly Orem, George Washington University—1930
Harry Byron Orleans, George Washington University—1932
Weldon Aubrey Price, Georgetown University—1934
William Gilmer Puryear, University of Virginia—1934
William Raffel, George Washington University—1935
Evelyn B. Reichenbach, Johns Hopkins University—1921
Isadore Rodis (Formerly Assoc.), Georgetown University—1928
Charles Pennington Ryland, Medical College of Virginia—1929
Frank James Shaffer, Jr., University of Michigan—1936
Frank Raymond Shea, Georgetown University—1929
Samuel Jacob Sugar, University of Maryland—1934
Richard Thornburgh Sullivan, George Washington University—1935
John Alden Swartout, New York Medical College—1936
George Tolstoi, George Washington University—1936
Thomas Frasier Williams, Tulane University—1930

For Associate Membership

Marian M. Crane, Johns Hopkins University—1928
Ralph Manning Crowley, Northwestern University—1934
Ethel Collins Dunham, Johns Hopkins University—1918
Edna Gerrish Dyar, University of Maryland—1930
Charles Chris Hageage, Georgetown University—1932
Maurice Crowther Hall (D.V.M.), George Washington University—1916
Robert Carhart Hood, Johns Hopkins University—1916
Virginia Elizabeth Lane, Woman's Med. Coll., Phila.—1928
Wesley Long Mays, University of Nebraska—1936
Benjamin Wallace Viton, Creighton University—1936
Dorothy V. Whipple, Johns Hopkins University—1929
William Robert Willard, Yale University—1934

Recent changes in membership status:

Active to Associate

Amanda L. Stoughton
Bernard J. Gurwin

COMMITTEE PERSONNEL

The President has appointed the following to serve on the Committee on Medical Economics:

Arch L. Riddick, *Chairman.*
Edgar M. McPeak, *Secretary.*

SUBCOMMITTEES

Coöperation with Government Agencies in Care of Indigent

B. W. Leonard, *Chairman*
R. Massie Page
Edgar P. Copeland

Coördination of Resources for Medical Care

Eugene A. Taylor, *Chairman*
Alva D. Daughton
John D. Wynkoop
Edmund M. Ellerson

Dissemination of Medical Economic Information

Robert E. Moran, *Chairman*
Howard P. Parker
Jack A. Connor
J. Burton Glenn
Linn F. Cooper

Government and Public Health Agencies

Oscar B. Hunter, *Chairman*
W. W. Chase
Raymond T. Holden, Jr.
Frank W. Braden
Thomas Bradley

Hospitals and Dispensaries

Henry L. Darner, *Chairman*
Earle G. Breeding
B. L. Hardin, Jr.
Edward M. Pickford
M. W. Glover
Saul Schwartzbach
William J. Cusack

Pursuant to resolution adopted by the Society, the President, Dr. Thomas E. Neill, has appointed the following Delegates to the Federation of Citizens' Associations to serve for a period of 1 year, beginning November 1:

Harry Lee Claud
John A. Logan

COMING MEETINGS

Wednesday, December 1: Business Meeting of the Society.

Thursday, December 2: *The Section on Neurology and Psychiatry.*

1. "Comparative Study of Arteriosclerosis and Hypertension." John P. H. Murphy, M.D.
2. "Control of Pain by Sympathectomy." O. H. Fulcher, M.D.

Wednesday, December 8: "Making Childbirth Safer." James M. H. Rowland, M.D., Dean and Professor of Obstetrics, University of Maryland School of Medicine, Baltimore, Md.

Tuesday, December 14: Joint meeting with the *District of Columbia Dental Society.*

"Marring and Mending the Human Face. A Study of How Health in Infancy Affects Facial Growth." T. Wingate Todd, M.B., Ch.B., Professor of Anatomy, Western Reserve University School of Medicine, Cleveland.

Wednesday, December 15:

1. "Intussuscepted Sigmoid—Blood Dyscrasia. A Case Report." P. A. McLendon, M.D., and Benjamin F. Dean, Jr., M.D.
2. "The Pathogenesis of Auriculoventricular and Intraventricular Heart Block." Wallace M. Yater, M.D.

Discussion: Walter A. Bloedorn, M.D.

Recess, Holiday Season.

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS

The regular meeting of the Washington Society of Pathologists, Inc., was called to order at 1:30 P.M., Saturday, October 2, 1937, in the Army Medical Museum by the President, Dr. Oscar B. Hunter. The minutes of the May meeting were read by the Secretary, Captain Elbert DeCoursey, and approved. There were 24 members and guests present. Dr. Oscar B. Hunter reported that on Wednesday evening, March 30, 1938, this Society would present the program before the Medical Society of the District of Columbia.

Presentation of Cases

Dr. George J. Brilmyer reported the case of a 41-year-old white man who had complained of weakness, loss of weight and loss of appetite for 6 months. He had been given theelin for his weakness without improvement. Bilateral areas of dulness were found in the lungs. The liver extended 4-finger breadths below the costal margin. There was a fixed mass in the left upper quadrant of the abdomen. At autopsy 3 living Trichinella larvae were found in 50 grams of diaphragm (0.06 Trichina larvae per gram of diaphragm) as well as an epidermoid carcinoma of the left kidney. The gross specimens and microscopic sections were demonstrated.

In the discussion the similarity of this epidermoid carcinoma arising from the epithelium of the renal pelvis to hypernephroma was noted.

Dr. R. M. Choisser presented the case of a white woman, aged 34 years, whose chief complaints had been pain in the head for 5 years, and loss of sight. The pain first radiated to the eyes and the temporal region; it increased in severity; during the last 2 years blindness had developed to the point where she could distinguish only light and darkness. There were occasional projectile vomiting, some loss of weight and for 4 years amenorrhea. She was well nourished. Her pupils were dilated and reacted to light and accommodation. Ophthalmoscopic examination showed optic atrophy. The breasts were large and pendulous and a milky fluid could be expressed from the nipples. The lungs and heart were negative. The blood pressure was 118 systolic and 90 diastolic. The temperature was 97°F. The abdomen was obese. No masses were palpable. The reflexes were equal and hyperactive; the Babinski was negative. The spinal fluid pressure was 14 mm. There was a surgical exploratory procedure on July 7, 1937, lasting 7 hours, during which the blood pressure fell to about 30 mm. Hg. Blood transfusion, adrenalin and pitressin were given to no avail and the patient died. The spinal fluid globulin was 35 Gm. Colloidal gold, X-ray of stomach and duodenum, Kahn test, urinalysis and X-ray of the chest were negative. X-ray of the skull showed poor outline of the sella turcica indicative of pituitary tumor. At autopsy there was dilatation of the third and fourth ventricles, but not of the lateral ventricles; complete erosion of the anterior and posterior clinoid processes of the sella turcica; pituitary gland replaced by a mass 3.5 by 2.5 cm., soft, which cut readily and showed a deep red hemorrhagic surface; no evidence of invasion of the brain. This mass peeled readily out of the sella turcica, which was considerably widened. The appearances suggested a pituitary tumor. The microscopic slides (which were presented) showed a peculiar alveolar arrangement, considered by some to be characteristic of chromophobe adenomas.

In the discussion, **Dr. Walter Freeman** said that "of real importance in differentiating pituitary tumors are the size of the cells and granularity of the cytoplasm; chromophile cells have a very definite granular cytoplasm. These cells are by no means granular and I do not see any definite evidence of malignancy."

Captain Elbert DeCoursey presented the case of a 72-year-old white woman who had had glaucoma for 10 years with gradual progression to total blindness. Two days after enucleation the husband for the first time told the doctor that his wife had complained of a lump in the right breast, but examination of the breasts did not reveal a tumor. Based on the classification in the Ophthalmic Registry as proposed by Callender, who divided melanotic tumors of the choroid, whether they are lightly or heavily pigmented, into 4 main types as revealed by their cell content: spindle-cell types A and B, epithelioid (which looks like epithelioma), fascicular (palisaded), and the mixed-cell types. In the Registry, among cases of melanomas, spindle-cell subtype A (without a nucleolus), there has not been a death from tumor. This case was classified as a malignant melanoma, mixed-cell type, of the choroid. Microscopic slides of the whole eye were shown.

In the discussion it was observed that the tumor had penetrated the sclera.

Dr. J. W. Miller presented slides of the lungs of a white man, 38 years of age, who had been confined to bed for the last 6 months of life because of weakness, dyspnea and unproductive cough. For the 12 years prior to death he had worked in the weaving room of an asbestos plant and previously had worked in a cotton mill for 7 or 8 years. This was a well-developed and typical case of asbestosis. The diffuse interstitial fibrosis and the presence of asbestosis bodies are characteristic of this condition. The differentiating feature of asbestosis as compared with silicosis is that in the former the fibrosis is diffuse, while in silicosis it is nodular.

In the discussion, **Dr. Miller,** answering a question, stated that the chemical analysis of the silica was not as high as in silicosis but it was above normal; in the right lung it was 0.61 per cent, and in the left, 0.76 per cent, which is 5½ times as much as is found in the normal lung. The use of polarized light is advisable for microscopic study of pneumokoniosis. No matter how slight the interstitial fibrosis one should always find the asbestosis bodies in cases of asbestosis.

Dr. George Tolstoi presented the case of a young man, 22 years old, who in the summer of 1936 developed weakness which had no relation to food habits. On May 15, a year later, he developed severe pain over the temporal region. On June 6 he developed acute pharyngitis and consulted a physician for the first time. All blood studies were negative. He made a fairly good recovery and went to Cumberland, Maryland. Again he was hospitalized and given blood transfusions. The spleen was enlarged, extending down to the iliac crest. A diagnosis of Banti's disease was made. Splenectomy was performed. Histopathologic examination disclosed Hodgkin's disease. The gross spleen and microscopic slides were shown.

In the discussion it was noted that there was no adenopathy in this case.

Dr. Roger M. Choisser presented a small tumor from the breast of a woman about 30 years of age. She stated that she had just noticed it during the preceding week. It was removed under local anesthesia and was a firm nodular tumor about the size of a pea.

In the discussion granuloma and carcinoma were considered as the diagnosis.

Dr. J. J. Weinstein presented the case of a patient who developed some swelling of the abdomen, was tapped and a chylous fluid obtained. Since then she had been tapped several times. A gland had been taken out 2 years before and the patient is now in Gallinger Municipal Hospital. She has lost about 50 pounds during the past few years. She has been sick for 5 years. The surgeon removed a very large soft gland with a rather smooth capsule, and on cut section the gland was very soft and smooth. No tumor was found, but the clinicians consider the case one probably of Hodgkin's disease with obstruction of the thoracic duct.

Dr. A. E. Wode presented two slides of a patient who came into the hospital on September 12 and went out on September 20. A "lipoma" of the scalp, about 4 inches across, was noted and was removed under local anesthesia. The mass was dissected out freely down to the skull, where it was attached to the bone. Spicules of the bone were removed. The tumor itself was about the size of a small orange, had a smooth surface, and was quite red, soft and mushy. A roentgenogram made after the mass was removed showed no involvement of the bone and no lesions anywhere in the body. The question was whether this was extramedullary or whether it involved the bone. The section showed the tumor to be composed of cells of uniform size and shape with some large forms with irregular nuclei and large nucleoli but generally resembling plasma cells.

In the discussion, neoplastic plasmacytoma was considered. The unusual picture of mitotic figures in plasma cells was noted.

Dr. L. H. Snyder presented microscopic slides of a papillomatous lesion about 1 cm. in diameter which was found accidentally at autopsy in the region of the pylorus in a white man, aged 45 years. The patient had had subacute bacterial endocarditis with typical lesions of the mitral valve. In the microscopic sections of the tumor were found large irregular glands and a marked dedifferentiation from normal. It resembled a papilloma of the stomach undergoing a rather early carcinomatous change, a very early papillary carcinoma perhaps.

In the discussion the consensus of opinion was that the tumor was malignant.

Dr. Henry L. Wollenweber presented an interesting case of melanosis coli.

In the discussion it was stated that the pigment was iron-negative, acid-insoluble, and regarded as true melanin. The pigment was confined to the colon.

The meeting adjourned at 4 P.M.

NEWS AND PERSONALS

The Health Officer, Dr. George C. Ruhland, asks the coöperation of the profession in bringing files of report cards on tuberculosis up to date. There are many report cards extending as far back as 1908 without any check as to the patient's present status. To clear the files those physicians who have reported cases of tuberculosis will receive from the Health Office a card on which it is urged that the desired information be given.

Subcommittee on Tuberculosis,
Committee on Public Health.

Dr. James A. Cahill, Jr., before the Clinical Congress of the American College of Surgeons, at the Stevens Hotel in Chicago, October 28, 1937, presented a paper with lantern slides, entitled "Complete Avulsion of the Scalp and Loss of Right Ear with Reconstruction by the Tube Graft Method."

Dr. Walter Rapaport, Associate Member of this Society, has been, according to recent reports, elected President of the Napa County (California) Medical Society.

The George Washington University Medical Society announces that the William Cline Borden Lecture will be given on the evening of December 18. Dr. Charles Gordon Heyd, of New York City, Past President of the American Medical Association, has been selected as the lecturer.

The Southern Medical Association's Thirty-first Annual Meeting will be held in New Orleans, November 30–December 1, 2, 3. The preliminary program includes the following members of the Society as participants:

Papers will be read by—

Harry S. Bernton. "Recent Developments in Allergy."

James A. Cahill, Jr. "The Possible Relationship of Chronic Cystic Mastitis to Malignancy."

Austin B. Chinn, jointly with Edward B. Vedder. "Is the Nerve Degeneration of Vitamin B Deficiency Caused by Inanition?"

Eloise B. Cram. "Studies on Oxyuriasis: IX. The Familial Nature of Pinworm Infestation."

William Thornwall Davis. "Highlights of the History of Ophthalmology."

Ralph M. LeComte and Eugene R. Whitmore. "Diagnosis and Treatment of Renal Cysts."

James Alexander Lyon. "Gastro-intestinal Disorders Simulating Heart Disease."

George M. McCoy. The Second Charles Franklin Craig Lecture on Tropical Medicine: "The History of Leprosy in the United States."

Earl B. McKinley. "Present Status and Significance of Skin Tests in Leprosy."

Eugene R. Whitmore. "Cysts of the Kidney."

Participants in formal discussion of papers include—

John Minor, discussion of paper by Lee Rice, San Antonio, Tex. "Primary Carcinoma of the Liver: A Report of Two Cases Associated with Cirrhosis."

James W. Watts, discussion of paper by Cobb Pilcher, Nashville, Tenn. "Bony Intracranial Tumors."

Scientific Exhibit:

J. Russell Verbrycke, Jr. Gallbladder Adhesions with a New Clinical Syndrome and New Diagnostic Method.

Henry William Jaeger, M.D.

(1888–1937)

Dr. Henry W. Jaeger, a native of Washington, was born March 14, 1888. He had been engaged in the general practice of his profession since completing his internship in German Hospital, Brooklyn, N. Y., in 1913, to the day of his death, October 21, 1937. He later served on the attending medical staffs of Casualty and Providence Hospitals. For some time he was attached to the outpatient staff of the George Washington University Hospital. His committee appointments in the Medical Society of the District of Columbia, of which he became a member on March 14, 1914, included: Legal Advisory Committee, 1927–1928; Civic Health Committee, 1928–1930; Committee on Diagnostic Clinics, 1929–1930; Annual Meeting Committee, 1933–1934. He was an associate member of the American College of Physicians. Dr. Jaeger is survived by his widow, Mrs. Bessie S. Jaeger; his mother, Mrs. Henry Jaeger; two daughters, Dorothy, who is in the third-year class of George Washington University School of Medicine, and Cynthia; a son, Henry W., Jr.; a sister, Mrs. Cleve Richardson, all of Washington; and a brother, Ferdinand, of Long Island, N. Y. His funeral, which was largely attended by his fellow-practitioners, was held on October 23 at St. Mark's Episcopal Church.

Gideon Brown Miller, M.D.

(1861–1937)

Dr. G. Brown Miller, who practiced his specialty of gynecology for a period of 40 years, was born in Laurel Mills, Rappahannock County, Virginia, December 27, 1861, his death occurring on November 1, 1937. He received the degrees of C.E., in 1886, and B.S., in 1887, at the Virginia Military Institute, and M.D., in 1890, from the University of Virginia. His postgraduate training in his specialty was most extensive: Johns Hopkins Postgraduate School of Medicine, 1893–1894; University of Leipsig Medical Department, 1896–1897. He served on the House Staff of Johns Hopkins Hospital for 6 years, ending his service in 1901. Upon coming to Washington he assumed important staff positions at Columbia, Emergency, and Garfield Memorial Hospitals, becoming an associate in gynecology at the George Washington University School of Medicine. His membership in the Medical Society of the District of Columbia dates from October 1, 1902. From time to time he rendered important service on various committees, notably, the Legal Advisory Committee and the Committee on Cancer Clinics, and frequently contributed scientific papers. His funeral was held at St. John's Episcopal Church on November 4. The following members of the Society acted as honorary pall-bearers: Drs. Robert W. Baker, Charles M. Beall, W. Sinclair Bowen, Thomas A. Claytor, Francis R. Hagner, H. J. Russell McNitt, William Mercer Sprigg, A. L. Stavely, John Allan Talbot, E. W. Titus, B. F. Weems, Prentiss Willson, and Sothoron Key. Dr. Miller is survived by two sons, G. Brown Miller and Lieutenant Frank B. Miller; a sister, Mrs. McCalla Boulware of Fredericksburg, Va.; and three brothers, James, J. R. Brooke, and D. Lyle Miller of Rappahannock County, Va.

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THE CHEMOTHERAPY OF CERTAIN INFECTIONS WITH SULFANILAMIDE AND RELATED COMPOUNDS*

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Up to 2 years ago serum therapy offered the only practical means of combatting certain infections due to bacteria. Browning in England and Morgenroth in Germany had attempted for many years to develop specific drugs for this purpose, but nearly all drugs which were highly active in the test tube were inactive in the infected animal. It is true that Morgenroth's optochin and other quinine derivatives fell just short of the mark. The recent development of compounds which are of low activity against organisms in the test tube but which possess marked curative power in the infected animal, therefore, opened the path for the drug treatment of several diseases against which no effective therapy was previously available.

In this new field mention should be made of the work of Feldt and of Collier who developed some compounds of gold and sulphur that were shown to possess curative action against pneumococci and streptococci. It was not until the announcement of the more effective Prontosil by Domagk that wide-spread attention was given to this field of chemotherapy. Confirmation of the curative action of Prontosil against streptococcic infections came rapidly both in the laboratory and in the clinic, from all parts of the world. In a short time Tréfouël, Nitti and Bovet at the Pasteur Institute demonstrated that the active agent in Prontosil was only a fraction of the molecule, namely, the relatively simple chemical para-aminobenzene sulfonamide or sulfanilamide.†

It is in the laboratory that the ground must first be cleared, and research in this field is proceeding chiefly along three lines: (1) mechanism of action, (2) study of this group of drugs in other infectious diseases, (3) efforts to obtain more effective or less toxic drugs for the purpose.

MECHANISM OF ACTION

When we reflect that in spite of years of research the mechanism of action remains obscure for such well-known chemotherapeutic agents as quinine, bismuth, mercury and emetine, it is small wonder that the mechanism of action of sulfanilamide and related compounds is still in doubt. Several facts, however, have been unearthed. Colebrook and Long have independently shown that the blood serum develops an increase in bactericidal power against streptococci as a result of sulfanilamide therapy. The stumbling block here is that this does not occur in mice, although the curative action is perhaps most marked in mice. Both Colebrook, and Long also demonstrated that sulfanilamide in 1 to 10,000 concentration inhibited growth of streptococci in the test tube if only a few streptococci were present. Tested in the routine way it is a very feeble germicide in the test tube, although Branham and I have shown rather marked bacteriostatic action on the pneumococcus and meningococcus. Levaditi believes the action is directly on the organism, antagonizing leukocidins and hemolysins, although other workers disagree; Long and Mellon could find no effect on phagocytosis. Veldee and I studied the effect in rabbits on the neutralization of the "skin" toxin of the streptococcus and found that no neutralization occurred either when the drug and toxin were mixed before injection into the ear, or when the rabbit was first administered the drug and then injected with the toxin. The local toxin reactions were just as severe as in the control experiments.

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* Address delivered at the Second Annual Alumni Extension Course of Georgetown University School of Medicine, September 13, 1937.

† Also marketed under the trade names Prontylin and Sulfamidyl.

The weight of evidence indicates that the mechanism of action is upon the organisms rather than a nonspecific effect upon the defense mechanisms of the body.

Effect of Sulfanilamide on Various Infections

Streptococci. Clinical results indicate that sulfanilamide is effective in all types of infection in humans with hemolytic streptococci.

In erysipelas the results are perhaps most striking; if treated early the course of the disease is usually checked within 1 to 3 days after full therapeutic doses of the drug have been given. Breen and Taylor in England report 35 cases, Meyer-Heine in France 150 cases, and Tonndorf in Germany 22 cases (treated with Prontosil). If those cases are excluded that were moribund or otherwise complicated before therapy was started, no deaths occurred in any of these treated cases.

In puerperal sepsis you are no doubt familiar with the results of Colebrook and Kenny; in 64 cases treated with Prontosil or sulfanilamide the mortality was 4.7 per cent as compared to a previous mortality of 24 per cent. Their mortality of 4.7 per cent in treated cases is close to that obtained by Long and Bliss in 70 cases of general sepsis due to hemolytic streptococci, in which the mortality was 5.7 per cent. Foulis and Barr on a series of 70 admissions treated 22 severe cases (11 had septicemia) of puerperal sepsis with only 1 death, a mortality of 1.4 per cent for the series.

Even more convincing are the results in streptococcic meningitis, a disease almost invariably fatal. Many of these cases can now be saved as is evidenced by only 1 death in 4 cases treated by Schwentker and Long; by 2 successfully treated cases reported by Weinberg, Mellon and Shinn, and 1 case reported by Anderson.

In scarlet fever the value of sulfanilamide therapy remains to be established. Experimental and clinical evidence would indicate it to be of benefit during the invasive phase of the disease (Peters and Havard; Whitby), but in the later stages of scarlet fever it should be used cautiously or withheld unless definite indications for its use are present.

In nonhemolytic streptococcic infections, notably bacterial endocarditis due to streptococcus viridans, sulfanilamide therapy has not yet been proven of value. From a few personal reports the only effect with which I am familiar is a temporary remission in fever, with no appreciable influence on the course of the disease. In this connection it is interesting that in the laboratory sulfanilamide has much less effect against organisms of low virulence than against those that are highly virulent and rapidly fatal (Nitti and Bovet).

Combined Drug and Serum Therapy

The relationship of drug therapy to serum therapy has interested us at the National Institute of Health. Against streptococcal infections there are two types of antiserum. One, such as the scarlet fever serum, neutralizes toxins but has no effect on the invasiveness of the streptococcus in the animal body; the other, such as the erysipelas serum, contains antibacterial factors and can under experimental conditions prevent death from streptococcus septicemia. It has been shown that sulfanilamide does not have an effect similar to the first type of serum, which neutralizes certain toxins. Does the drug act in a manner similar to the second type of serum, to prevent invasiveness of streptococci?

We have performed experiments (hitherto unpublished) comparing drug therapy with serum therapy against streptococci isolated from human cases of erysipelas, scarlet fever, general septicemia. It must be remembered that in mice all 3 organisms cause death by septicemia.

In our experiments both scarlet fever antiserum and normal horse serum had no influence on the fatal streptococcic septicemias of mice. The antibacterial (erysipelas) serum had a distinct effect in preventing death from these infections even when administered 5 hours after the inoculation; this effect, however, varied considerably with the strain of streptococcus used.

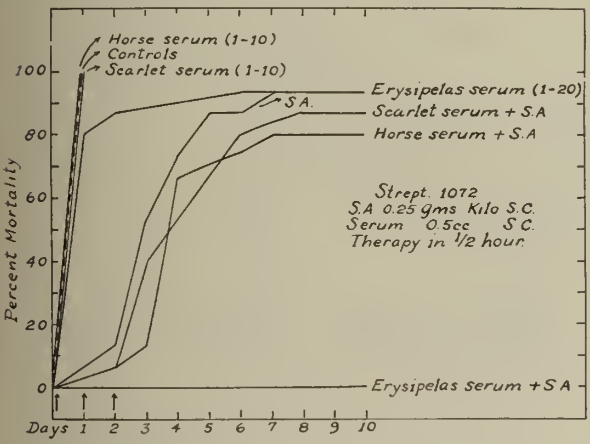

FIG. 1. The synergistic action of sulfanilamide and serum (antibacterial) therapy in experimental streptococcus septicemia in mice; 10 mice to each group; dosage of serum and drug adjusted so that either alone had little curative action; combination therapy yielded a high per cent of cures; treatment given at times indicated by arrows; streptococcus originally isolated from a case of scarlet fever; similar results obtained with streptococci isolated from erysipelas and from general sepsis.

The dosage of serum and of sulfanilamide was adjusted so that few or no mice survived the streptococcic infection as a result of either type of therapy used alone. In the same experiments the combination of drug and serum therapy was also employed in a group of infected mice.

It will be seen from these experiments that scarlet fever serum has little more effect in reducing mortality than has plain horse serum when combined with sulfanilamide therapy (Fig. 1). However, the combination of an antibacterial serum with drug therapy gives a distinct reduction in mortality over that from serum or drug alone. The reduction is greater than an addition of effects—a real synergistic action; this is evidence that drug therapy and serum therapy operate through different mechanisms of approach so that they can mutually augment each other. Similar results have been previously obtained by Meyer. This finding should have practical significance, for in patients very ill with streptococcus septicemia a combination of serum and drug therapy should bring about a reduction in mortality below that which can be obtained from either type of treatment used alone.

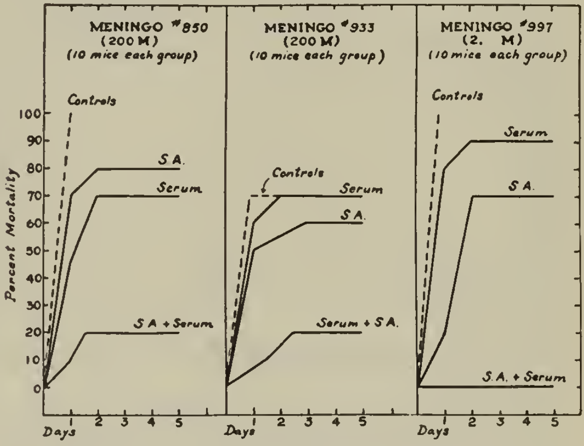

FIG. 2. Three experiments with meningococcus infections showing the marked curative effects of combined drug and serum therapy where each alone yielded poor results; treatment S. C. 2 hours after infection with 0.8 Gm. per kilo of sulfanilamide and 0.5 cc. of 1 to 5 dilution of meningococcic serum.

MENINGOCOCCIC MENINGITIS

Buttle first showed experimentally that sulfanilamide could prevent death from meningococcus infections, and this finding was confirmed and elaborated upon by his associate Proom, who demonstrated marked curative action in mice if treatment was begun within 5 hours after inoculation. For mice this is relatively late in the disease, since many of the animals die within 12 to 18 hours after infection. Branham and I studied the effect of sulfanilamide therapy upon 20 strains of meningococci and found curative action in all, but some strains were much more resistant to treatment than others. Where drug treatment gave poor results the combination of drug and serum treatment always brought about the survival of most of the infected mice (Fig. 2). Although death in mice is from septicemia rather than meningitis, I believe that this evidence suggests the value of combination therapy in the clinical treatment of meningococcic meningitis.

In the rapidly fatal course of Meningococcus infections in mice we also found that subcutaneous therapy gave better results than oral administration, a fact that should be remembered when urgent treatment of very sick people is called for. As to the intraspinal injection of the drug, I believe the dangers are not yet sufficiently known, and would limit the treatment to oral or subcutaneous routes, except perhaps in such desperate conditions as streptococcic meningitis.

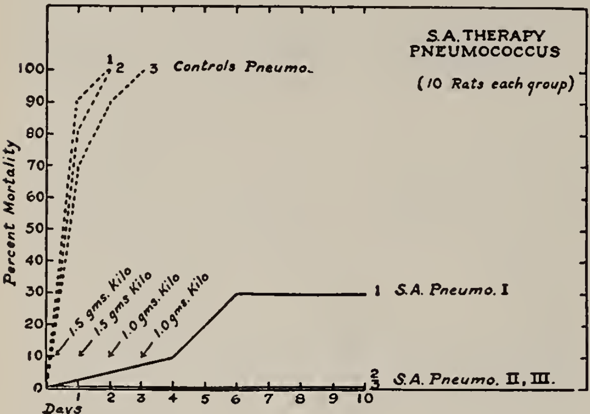

FIG. 3. The curative action of sulfanilamide in pneuomcoccus Types I, II and III infections in rats; infection intraperitoneally; treatment subcutaneously at times indicated by arrows.

Schwentker, Gelman and Long have reported 10 human cases of meningococcic meningitis treated with sulfanilamide orally and intraspinally, with 1 death, and I have been informed of other larger series of treated cases in which favorable results have been obtained.

PNEUMOCOCCUS PNEUMONIA

At the National Institute of Health we first demonstrated that sulfanilamide possessed a slight but definite curative effect on mice infected with pneumococci of Types I, II and III. In rats this action is more marked and a high degree of cures can be brought about as a result of therapy (Fig. 3). This was shown at the same time independently by Gross and Cooper for Type III pneumococcus. These investigators have subsequently reported a series of 13 human cases of Type III pneumonia treated with sulfanilamide with 2 deaths. From present knowledge, however, I do not anticipate a great reduction in mortality in pneumonia from sulfanilamide treatment alone, but there is reason to believe that the combination of drug and serum therapy will materially lower the number of deaths from pneumococcus pneumonia. Both Gross and Cooper and ourselves were able to demonstrate a synergistic action of drug and serum in combatting Type I pneumococcus infections in animals (Fig. 4).

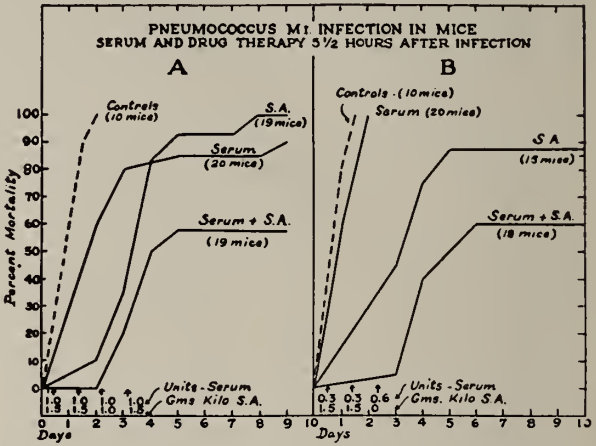

FIG. 4. The increased effectiveness of combined drug and serum therapy in Type I pneumococcus infection in mice; units of serum (Felton) and dosage of sulfanilamide indicated by arrows on the chart.

TYPHOID AND PARATYPHOID FEVERS

Although there are as yet no clinical reports available to evaluate sulfanilamide therapy in typhoid and paratyphoid fevers, the experimental evidence of Buttle suggests its use here. These observers found upon infections in mice that the greatest curative value of this drug was shown upon the meningococcus and typhoid organisms; the streptococcus comes next in the ease with which it may be attacked by sulfanilamide therapy. In a third group with which partial protection can be achieved are the pneumococcus, Friedlander bacillus, *B. aertryke*, *Pasturella septica*, and Staphylococcus. To this list may now be added the gonococcus (Reuter; Dees and Colston) and the gas bacillus.

GAS GANGRENE

Bohlman of Baltimore reports 2 cases of this disease treated with sulfanilamide with dramatic results. Long has brought forth laboratory evidence to serve as a basis for its effect on the Welch bacillus, and it is hoped that future experience will bear out these promising results.

STAPHYLOCOCCUS

In the clinic results have been variable in the treatment of staphylococcus septicemia. Its final worth remains to be established. In the laboratory difficulties have been met in obtaining strains pathogenic for animals, but where such strains have been found, curative value has been demonstrable. From present evidence we may expect some benefit in staphylococcus infections but to a less extent than with the streptococcus.

CHORIOMENINGITIS VIRUS

Wooley, Bauer and I have been able to show an effect on choriomeningitis infection in mice. Curiously, this action was possessed only by the original Prontosil of Domagk (Fig. 5). These studies have as yet no practical value but are reported to show that some virus diseases may ultimately be brought under the influence of this field of chemotherapy.

TOXICITY

I have reported all of these promising results with sulfanilamide, but now it becomes necessary to say things less encouraging. To materially benefit severely ill patients large doses of sulfanilamide are necessary; it is becoming clear that in nearly every instance some toxic results, either mild or severe, occur when these large amounts of the drug are given. It should always be borne in mind that toxic manifestations are more prone to occur in patients who are severely ill. Acidosis is the most frequent disturbance and probably occurs to some degree in all cases in which large doses are used, as Southworth has shown. To combat this acidosis sodium bicarbonate in doses equivalent to those of sulfanilamide should be employed. Fever due to the drug occurred in 15 per cent of 134 cases reported by Hageman and Blake; characteristic of this fever is an onset usually 7 to 10 days after therapy has been started. Skin rashes occur in about 10 per cent of cases,* often in association with the fever. Both sulfhemoglobinemia and methemoglobinemia occur with rather irregular frequency; in studies made by some observers it is commonly present (Paton and Eaton); with other observers it has been entirely absent. Archer and Discombe believe that spectrographic examination of the blood is very helpful. Methemoglobinemia disappears within a day after treatment is discontinued, but sulfhemoglobinemia is more serious and more persistent. They believe that the sulfhemoglobin arises from the hydrogen sulfide absorbed from the alimentary tract, the drug acting as a catalyst to its combination with hemoglobin. They suggest the following preventive measures: (1) Diminution of H_2S formation in the large

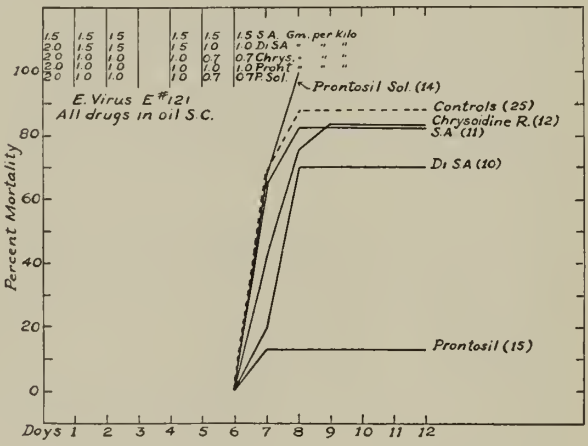

FIG. 5. Comparative results with choriomeningitis virus infection in mice; only Prontosil effective. (Dosage of drugs shown on chart. The numbers of mice used are shown in parentheses.)

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* Since this was written further reports of dermatitis, of anemia, and of optic neuritis have appeared in the J. A. M. A., September 25, 1937.

intestine by a low residue diet containing few eggs, (2) avoidance of cathartics during therapy except 1 to 2 ounces of mineral oil, and (3) cleansing the colon with an enema at the onset of therapy. Antagonistic to their observations are those of Marshall who could not account for the cyanosis by the presence of methemoglobinemia.

Nausea and vomiting and dizziness are frequent, and I am told several automobile accidents have already occurred as a result of the administration of sulfanilamide to ambulatory patients who subsequently drove their cars.

Cases of acute anemia and of neutropenia have been reported (Harvey and Janeway), and a close study of the blood picture should be made in all patients receiving sulfanilamide for any length of time.

Little is known of the possible chronic effects of the drug, but the report of a case of agranulocytosis following treatment (Borst) demonstrates the possibility of such effects.

Therefore, it becomes clear that the indiscriminate use of this drug should be discouraged. One should first be sure that the type of infection indicates its use, then that its use is necessary. In acute diseases with high mortality rates such as septicemia and meningitis, the dangers from the use of the drug are remote as compared to the dangers from the infection, and sulfanilamide should be given in large doses—0.1 gram per kilo or 7 5-grain tablets for each 50 pounds body weight per day, with equal quantities of sodium bicarbonate, until improvement occurs or until toxic manifestations require that the drug be discontinued or the dosage reduced.

The work of Marshall and of Fuller is of value in increasing our knowledge of the absorption and excretion of sulfanilamide and in demonstrating that a considerable fraction is acetylated as it passes through the human body. When the drug is given by mouth, a concentration of sulfanilamide in the blood of 5 to 10 mg. per 100 cc. has been established as a satisfactory level for therapeutic response, but these levels are not always attained within the limits of the usual dosage, nor can they always be maintained over a period of time without the development of toxic manifestations.

DEVELOPMENT OF NEW DRUGS

With the increasing evidence of toxicity of sulfanilamide a wide-spread endeavor to find more suitable compounds has been undertaken. The course of events will now pass from the stage of enthusiasm to the stage of confusion. This will be in part caused by the efforts of drug firms, each to further their individual products, and in part by the difficulty of establishing the relative value of different compounds because of varying laboratory conditions and because of the absence of a standardized experimental technic. Many new compounds will be made available commercially, and much work will be necessary in the laboratory and in the clinic before their relative merits are established.

More effective and less toxic compounds are being developed, and along with this some promise is shown that specific drugs will be found which have selective action against certain diseases.

In comparisons carried out at the National Institute of Health sulfanilamide was found to be more effective than Prontosil or Prontosil Soluble, and a new compound di-sulfanilamide, prepared by Hugo Bauer, was shown to be twice as effective and approximately one fifth as toxic as sulfanilamide. In Europe the benzyl derivative of sulfanilamide (Setazine) has had extensive use, particularly in France (Bloch-Michel, Conte and Durel; Peters and Havard). It is definitely of lower toxicity.

Until recently the most active compounds had as their basis a sulfonamide group and an amino group in the para position in the benzene ring, and it was thought that these chemical groups or their substitution products were essential to chemotherapeutic action. However, developments announced simultaneously by Buttle in England and Fourneau in France reveal that highly active compounds have been obtained which do not necessarily contain either of these groups and which are so constituted chemically that the possibility of conversion into sulfonamide compounds in the body is remote (Fig. 6). One of these compounds, di-amino-diphenyl sulfone, is a great deal more active than sulfanilamide but also more toxic.* The acetyl derivative of this product has given especial promise against pneumococcic infections (Fourneau, Tréfouël, Nitti and Bovet). Another compound, di-nitro-diphenyl sulfone, is as active but less toxic. These findings demonstrate that chemical progress can be made along a wide front, just as biological advances may be expected to bring under the influence of chemotherapy an increasing number of infectious diseases.

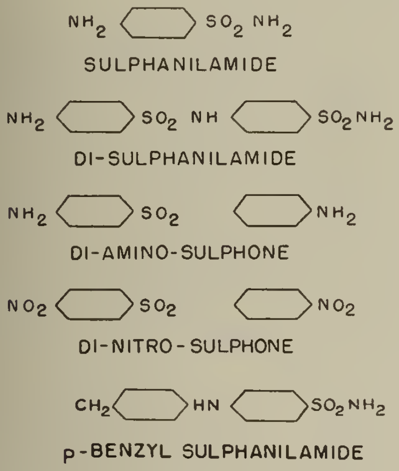

Fig. 6. New compounds of promise in the chemotherapy of certain bacterial infections.

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*Bauer and Rosenthal have prepared a soluble formaldehyde sulfoxylate derivative of this compound which shows promising experimental results upon streptococci and pneumococci (U. S. Pub. Health Rep., in press).

FACTORS IN THE PRODUCTION AND TREATMENT OF SHOCK: AN EXPERIMENTAL STUDY*

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Historical Introduction

Shock, exemia or circulatory collapse was recognized in the days of the early Greek and Roman Empires. However, the nature of the condition remained hidden for many centuries. In 1664, Ambroise Paré described the state of primary shock under the terms of syncope and heart failure. Progress toward an understanding of shock was slow, but was perceptibly accelerated by various wars in Europe. The work of Hunter, Cooper, and Travers during the eighteenth century is of interest. Latta, in 1795, was the first to apply the term "shock" to the entity. Toward the end of the nineteenth and commencement of the twentieth centuries, interest in the subject was stimulated by the studies of Bainbridge and Trevan, Mitchell, Keen, Crile, Porter, Groeningen, and Henderson. The Great War (1914–1918) with its wealth of clinical material was the starting point of more recent investigations. The coöperation of American, British, and French surgeons and physiologists in the study of shock with the subsequent establishment of study stations at Dijon and Béthune laid the foundation of present-day concepts of the shock syndrome.

Concepts of the Shock Syndrome

The manifestations of shock, the general apathy, the pallor of the skin, the profuse sweating, the slow sighing respirations, the fall of blood pressure, the rapid feeble pulse, the reduction of blood volume, the raised blood sugar and nonprotein nitrogen, the acidosis, the leukocytosis, the diminished metabolic rate, the concentration of the red blood cells, the increased blood viscosity, the diminished volume flow of blood, and the peripheral vasoconstriction are too well known to require further elaboration here. An increasing mass of knowledge has resulted in the evolution of certain hypotheses regarding the underlying mechanism, each of which present a facet of the total problem. In order to clarify the investigational approaches used in this study, a brief statement of the main concepts may be pertinent.

1. The blood in shock becomes stagnant in the large venous reservoirs of the chest and abdomen (Fischer). Although, in experimental shock produced by repeated trauma to the intestines, as much as 37 per cent of the total blood volume may be "pooled" in the splanchnic area (Mann; Gasser, Erlanger and Meek), the clinical observations of most surgeons (Wallace, Fraser and Drummond) do not indicate the presence of splanchnic congestion in shock.

2. Fat embolism. It has been suggested (Warthin, Groeningen) that embolic particles of fat released from the area of trauma may reach the central nervous system and lungs resulting in a state of shock. However, histologic studies do not lend any weight to this concept.

3. Vasomotor paralysis. This concept, sponsored by Mitchell and by Keen, suggested that the symptoms of shock resulted from exhaustion or paralysis of the vasomotor centers. Later Crile made it the basis of his work upon anociassociation. No confirmation of this hypothesis comes from the work of Mann and others, who have found that prolonged stimulation of an afferent nerve trunk does not cause a fall of blood pressure.

4. Adrenal hyperactivity. The experimental injection of large quantities of adrenalin causes shock accompanied by a concentration of the red blood cells (Bainbridge and Trevan, Erlanger and Gasser). Estimations of the adrenalin content of the blood in shock do not suggest its presence in such quantities as to intensify the con-

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* Abstract of The Davidson Lecture delivered before the Society, October 13, 1937.

dition (Stewart and Rogoff). Recently it has been stated that in the "sham rage" of decorticate animals a reduction of the blood volume takes place as a result of overactivity of the sympathetic nervous system (Freeman). This has been confirmed (Gregersen).

5. Acapnia. Henderson suggested that the excessively deep and rapid respirations resulting from painful stimuli produce a diminution of the CO_2 content of the blood. The respiratory center is no longer stimulated, and shock follows. In clinical shock the breathing is rapid but shallow, while the CO_2 content of the blood is decreased (Cannon; Crile; Clark; Mitchell).

6. Vasoconstriction and capillary congestion. In shock a condition of generalized vasoconstriction is present causing a stagnation of the red blood cells in the capillaries and the passage of blood plasma into the tissue spaces (Malcolm; Starling; Erlanger and Gasser).

7. Traumatic toxemia. Vasotropic substances are released from the area of trauma and act upon the capillaries throughout the body causing them to become more permeable so that blood plasma escapes and an oligemia occurs (Cannon and Bayliss; Dale and Richards; Grunke and Haring). Later observers have been unable to obtain toxic substances from areas of trauma (Simonart; Blalock; Roome and Wilson; Schneider; Herbst). Recently an increased amount of histamine in the venous blood from traumatized limbs has been noted (Minard).

8. Local fluid loss. Careful weight measurements of traumatized areas indicate that the reduction of blood volume may be entirely accounted for by a loss of blood and serum into the tissues at the site of trauma (Blalock; Parsons and Phemister).

Classification of Shock

Shock may be divided into primary shock and secondary shock, but the basis of differentiation must be one of difference in etiology rather than difference in time of occurrence. Primary shock is produced by the action of psychogenic or neurogenic stimuli upon the medullary centers resulting in a loss of vasomotor tonus, especially in the splanchnic region. This is well illustrated by the Goltz experiment. A fall of blood pressure takes place accompanied by bradycardia, pallor and faintness. No reduction in the blood volume is present. Secondary shock, on the contrary, is accompanied by oligemia. In this study the problem of secondary shock has been viewed from three standpoints:

1. The tissue changes resulting from trauma and hemorrhage.
2. The regional redistributions of blood volume following trauma and hemorrhage.
3. Delimiting factors in the therapy of secondary shock.

Tissue Changes in Shock

A study of the tissue changes in shock was made to determine (1) whether or not shock produced by trauma is similar to that produced by hemorrhage, as evidenced by the histopathologic changes, and (2) whether the tissue changes in adrenalin shock could substantiate the theory of excessive adrenal activity in shock. Shock was produced by four methods:

1. Repeated trauma to both hind limbs.
2. Repeated hemorrhage.
3. Injections of histamine hydrochloride.
4. Injections of adrenalin.

The tissue pathology was found to be similar in shock produced either by trauma or by hemorrhage. The peritoneal cavity contained a variable amount of protein-laden fluid which was often blood-stained. The gastro-intestinal tract was relaxed and flabby, and constriction of the arterioles was present. No evidences of splanchnic congestion were found. The changes in the heart were variable depending upon the total blood volume present at the time of death. If the blood volume was much diminished the heart was small and contracted. If the blood volume was relatively normal, as in adrenalin shock, the heart was dilated. The lungs showed varying degrees of edema depending upon the duration of the shock state, and, where shock was prolonged, the edema was great.

In shock produced by adrenalin the tissue changes do not resemble those produced by hemorrhage or by trauma. The lungs are usually very edematous. The heart is always dilated. The liver shows frequently areas of vacuolation of the hepatic cells with foci of central necrosis. This is not observed in shock resulting from trauma or hemorrhage. In adrenalin shock the thyroid gland shows a vacuolation and some disappearance of the colloid in the acini and a mild hypertrophy of the lining epithelium. In histamine shock there are evidences of extreme vascular congestion in the splanchnic and thoracic viscera.

In conclusion, it may be stated that the histopathologic appearance is the same both in traumatic and hemorrhagic shock, which suggests that the basic etiology is similar. The tissue changes present in adrenalin shock differ from those of hemorrhage and trauma, and this does not lend support to the concept of an excessive adrenal activity playing the major rôle in secondary shock.

REGIONAL REDISTRIBUTION OF BLOOD VOLUME IN SHOCK

Implicit in the concept of physiological homeostasis (Cannon) is the occurrence of translocations of blood volume in response to normal and urgent stimuli. In this phase of the investigation an effort was made to determine quantitatively the regional redistribution of blood in the intact animal in a state of shock with particular reference to the theory of "splanchnic pooling" of blood. By the use of a specially designed apparatus, the head, thoracic, abdominal and peripheral (hind limb) areas of nembutalized dogs were weighed before and during the production of secondary shock. It was found that trauma is associated with a loss of blood volume into the traumatized area which gains in weight. Simultaneously blood is lost from the cephalic, splanchnic and thoracic regions. However, if the duration of the condition is prolonged, a secondary increase in weight of the thoracic area takes place as a result of edema of the lungs. In shock produced by hemorrhage the greatest loss is from the splanchnic area and to a lesser extent from the thoracic and cephalic regions. As the state of shock continues, an increase in weight takes place in the hind-limb region due to a peripheral pooling of blood. In histamine shock, blood is shifted into the thoracic and abdominal areas, while it is lost from the periphery and from the head. These findings, based upon direct experimental evidence, do not provide any basis for the theory of a splanchnic pooling of blood in traumatic or hemorrhagic shock. However, they do provide a further differentiation of histamine shock from shock of traumatic or hemorrhagic origin. They suggest, furthermore, that a slight "pooling" of blood does occur into the blood vessels of the muscles.

FACTORS IN THE TREATMENT OF SHOCK

In this phase of the investigation there were considered:

1. The physiological availability of fluids in secondary shock.
2. The physiological effects of induced vasopression in secondary shock.

PHYSIOLOGICAL AVAILABILITY OF FLUIDS IN SECONDARY SHOCK

An investigation was undertaken to determine the nature and mechanism of the response of normal and shocked animals to water and electrolytes. In view of the fact that the central phenomenon of shock is an anoxemia which is the resultant of such factors as oligemia, lowered blood pressure, diminished volume flow of blood, and peripheral vasoconstriction, it was decided that the rate of oxygen consumption of the animal would provide a more accurate picture of the tissue effects of secondary shock. Dogs were used throughout and the metabolic determinations were made by means of a Krogh respiratory apparatus.

In normal animals the intravenous injection of isotonic sodium chloride solutions increases the rate of oxygen consumption by 25 to 50 per cent. The maximal increase is reached only after 1400 to 2400 cc. of fluid has been given. Thereafter, a plateau in the curve is obtained, and this is maintained so long as the fluid is injected and for some time afterwards. The tolerance for water is great in normal healthy animals. Fluid to the extent of 25 per cent of the total body weight of the animal may be given without any deleterious result. In traumatic and hemorrhagic shock, however, a peculiar alteration of the metabolic response to fluids occurs. The maximal increase in the rate of oxygen usage is reached at an earlier stage of the fluid injection, i.e., after 700 to 1200 cc. of the solution have been given. Thereafter, the administration of fluids results in a progressive decline in the rate of oxygen consumption. In secondary shock, the tolerance for fluids is much diminished, because the administration of a quantity of water equivalent to only 5 to 12 per cent of the body weight produces a fall in the metabolic rate. Not only is there an alteration of the metabolic response in secondary shock, but renal function also is affected, inasmuch as water diuresis is minimal, even after large infusions.

NATURE OF THE ANOXEMIC RESPONSE

A diminution of oxygen usage after fluid administration may result from:

1. Insufficiency of oxygen available to the blood in its passage through the lungs.
2. Decrease of available oxygen-carrying material in the blood stream.
3. Interference with the oxygen utilization of the tissue cells.

The third factor was excluded in view of the fact that the administration of large quantities of fluids sufficient to produce obvious generalized edema in normal animals causes no decrease in the oxygen consumption rate.

Two subsidiary investigations were undertaken: the first, to determine whether or not the injection of fluids into the shocked animal could produce edema of the lungs sufficient to interfere with passage of oxygen from the alveoli into the blood; the second, to determine whether or not the administration of fluid could result in a loss of blood protein and cells into the tissue spaces. It may be stated, briefly, that the experimental data did not support the assumption that the anoxemia of shock resulted from pulmonary edema or that edema of the lungs was a significant factor in the production of the anoxemia following the injection of fluids into shocked animals. However, examination of the peritoneal transudates following the administration of fluids in normal and shocked animals revealed a loss of over 9.5 per cent of the total blood protein. Moreover, similar losses occurred into the areas of trauma. It is suggested, therefore, that the augmentation of the anoxemia of traumatic shock by fluids is the result of loss of protein and cells into the traumatized area, the peritoneal cavity and to a lesser extent into the alveoli of the lungs and general tissue spaces (Davis).

PHYSIOLOGICAL EFFECTS OF INDUCED VASOPRESSION IN SHOCK

In the tissues of the body there is a varying degree of sensitiveness to lack of oxygen (Pike, Guthrie and Stewart). Muscular and glandular tissues can withstand anoxemia for long periods. The central nervous system, and particularly the small pyramidal cells of the cerebral cortex are extremely sensitive to lack of oxygen (Gomez and Pike). The importance of the time factor in the development of shock is self-evident, and has been investigated (Porter, et al.; Cannon and Cattell; Lacroix; Pike and Coombs).

During an investigation of the local fluid loss resulting from trauma, a pressor phenomenon was noted following the injection of hypertonic solutions into the arterial system (Davis, et al.). This phase of the study concerned the mechanism of the pressor phenomenon and its application to experimental shock. The intra-arterial injection of 5 to 10 cc. of a hypertonic solution resulted in an elevation of the systolic blood pressure from 10 to 50 mm. Hg. above the initial level. The duration of this pressor phenomenon varied from 1 to 3 hours, or even longer. The arteries used were either the femoral or brachial. The effectiveness of the solutions used was variable. Sodium chloride (25 per cent) solutions were most effective, whereas solutions of gum acacia (30 per cent) had but little effect. Control solutions of isotonic sodium chloride did not increase the blood pressure. The intravenous injections of hypertonic solutions, in contrast to the intra-arterial, produced a depression of the blood pressure with a return to the initial level within 3 to 5 minutes. Total section of the spinal cord completely abolished the pressor reaction. Following bilateral adrenalectomy, the pressor response to intra-arterial hypertonic solutions took the form of a more gradual elevation of blood pressure which, however, was maintained.

The next step was the utilization of this pressor action in states of experimental secondary shock produced by trauma and by hemorrhage. The intra-arterial injection of small quantities (10 cc.) of a hypertonic sodium chloride solution (25 per cent) was effective in elevating the blood pressure which had been depressed by trauma and hemorrhage. The pressor action was rapid in onset, and a plateau was reached within a few minutes. Occasionally, a secondary slight depression of blood pressure followed the primary rise, but subsequently a further rise occurred. The most satisfactory results were obtainable where the state of shock was maintained for periods not longer than 20 to 30 minutes. It was found that the duration of the pressor response varied from 1 to 3 hours. Thereafter a gradual fall took place. A study of the fluid loss into the traumatized area indicated that the later decrease of blood pressure was associated with, and probably due to, a gradual effusion of blood serum into the site of trauma. At an early stage of this study it was believed that the pressor response resulted from withdrawal of the effused fluid from the traumatized limbs. A temporary withdrawal of fluid from this area did occur, but this did not appear to be of importance in the production of the vasopressor reaction. It has been demonstrated (Davis, et al.) that this phenomenon is of neurogenic origin. Injection of the solution into the arteries of non-traumatized extremities likewise raised the blood pressure in the presence of shock. A gross and microscopic examination of the injected arteries was made, but no evidences of thrombosis could be found. However, small hemorrhages were sometimes present between the adventitial and muscular coats of the artery. The result of the intravenous injection of a hypertonic solution into normal animals was a fall of blood pressure with a rapid return to the initial level (Davis, et al.). However, in secondary shock, the depressor effect was more striking, and might be fatal, while the secondary rise was delayed.

It has been demonstrated that in all forms of shock vasoconstriction is present. The present investigation suggests that, in the earlier stages of experimental shock, at least, such a vasoconstriction is beneficial, and its accentuation by means of the intra-arterial administration of hypertonic solutions is of value, inasmuch as the elevation of blood pressure is accompanied by a more adequate blood flow to the vasomotor and respiratory centers as evidenced by the disappearance of Traube-Hering waves and dyspneic respirations. The injection of adrenalin into shocked animals was found to be highly unsatisfactory in this study, for the elevation of blood pressure is transient, and is followed by depression below the initial level within 5 minutes. The method under investigation may prove useful eventually as a simple emergency treatment for secondary shock where more adequate treatment is not immediately available, and where the maintenance of a satisfactory blood flow to the central nervous system during the intervening few hours may render subsequent therapy more effective. However, it must be stated emphatically that this method is not yet ready for clinical application, and that further experimental work is being carried out to determine its limitations and possible dangers.

Conclusion

An investigation of certain factors, both pathological and physiological, in the production and treatment of secondary shock has been presented.

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The Physician and His Prescriptions.—For some time it has been observed that many physicians have become indifferent about prescription writing, and have developed a tendency to prescribe certain proprietary products in preference to official preparations. Some observers have said that this diminished use of official preparations is the result of the lessened time and effort in teaching therapeutics in medical schools of the country, and that the young physician gets a significant part of his training in therapeutics from the advertising material of the drug manufacturers. Perhaps such criticism of medical curricula has been justified in certain instances, but at present there is a very definite trend toward the proper emphasis on therapeutics in the medical schools. This is being accomplished by a better understanding and coöperation between the clinical and pharmacological departments. . . .

Flavoring with Adjuvants. The physician who prescribes his medication so as to make it look appealing and taste pleasant usually wins the gratitude of his patient. To supply medicines in palatable form is a part of the art of the pharmacist.

In this article the attention of physicians is called to a wide variety of vehicles available for conveying and flavoring official drugs; and the physician's attention is directed to the fact that the modern pharmacist is well qualified to furnish information on the best methods of supplying official drugs which the physician may wish to prescribe. . . .

Elixirs. A nationally conducted survey of 10,000 prescriptions, the results of which have been published, proves that the elixirs are very popular adjuvants. Of this class of preparations there are only two in the U. S. P. XI, namely, aromatic or simple elixir, and elixir of licorice. These are used as vehicles, and the elixir of licorice is especially useful in masking a dose of bitter drugs. In the National Formulary the following elixirs are listed:

1. *Aqueous Elixir* (*Elixir Aquosum*), prepared to meet the demand for a vehicle of the elixir type but without alcohol. It is colorless and has a pleasant taste.

2. *Red Aromatic Elixir* (*Elixir Aromaticum Rubrum*). The N. F. has simply transformed well-known, colorless, aromatic elixir of the U. S. P. into a bright red elixir. From a psychological viewpoint, this is frequently desirable. It contains about 23 per cent alcohol.

3. *Elixir of Bitter Orange* (*Elixir Aurantii Amari*). This elixir has a yellow color, and a delightful taste, and is valuable where a high alcoholic content is desired.

4. *Compound Elixir of Cardamom* (*Elixir Cardamoni Compositum*). This elixir is colorless and contains about 8 per cent alcohol. Its predominant flavor is cardamom.

5. *Compound Elixir of Vanillin* (*Elixir Vanillini Compositum*). An amber-colored elixir with a very delightful odor and taste, making it one of the most palatable elixirs of the vehicle group. It contains about 8 per cent alcohol.

Syrups. Syrups, because of their intense sweetness and heavy body, are particularly useful as vehicles for salty substances. . . . The advantage of acacia lies in the collodial nature of the product which permits dispensing of disagreeable substances and prevents them from coming in contact with the taste buds. . . . Patients like changes in the tastes of medicines. Syrup of cherry carries iron medication nicely. This fruit flavor is especially useful with sour substances, and is ideal for such materials as diluted hydrochloric acid or diluted hydriodic acid. *Syrup of Prepared Cacao* (*Syrupus Cocao Praeparati*), chocolate syrup, as it is commonly called, is very thick, creamy, and smooth. Therefore, it is frequently employed as a vehicle for the quinine salts. . . . *Syrup of Raspberry* (*Syrupus Rubi Idaei*).—This is one of the most palatable syrups of the N. F. It has a deep red color, and is particularly useful as a vehicle with acid preparations.

Abstract of article by Chester I. Ulmer, M.D., Gibbstown, N. J., and Robert P. Fischelis, Phar. D., Trenton, N. J., *Journal, Medical Society o New Jersey, November, 1937, p. 673*

ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY TUBERCULOSIS*

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Artificial pneumothorax may be defined as collapse of one or both lungs which is induced intentionally by the injection of air into the pleural cavity or cavities. Its chief use as a therapeutic agent is in the treatment of pulmonary tuberculosis, but it has been used to a lesser extent in the treatment of other conditions, such as pulmonary abscess, lobar pneumonia, unresolved pneumonia, bronchiectasis, and massive hemorrhage from the lungs. This discussion shall be limited to its use as a therapeutic measure in pulmonary tuberculosis.

In the induction of artificial pneumothorax air is injected into the pleural cavity in measured amounts at intervals. No attempt is made to collapse the lung quickly. Rather, an attempt is made to obtain a gradual collapse, maintaining as a rule subatmospheric intrapleural pressures. The reason that a gradual collapse is deemed more desirable is that it allows time for the development of several compensatory mechanisms which come into play when a lung is collapsed. In this way the alarming symptoms which frequently attend a spontaneous collapse of a lung are obviated. Superatmospheric intrapleural pressures should never be used in uncomplicated artificial pneumothorax. They may be used, however, with caution when it is desired to stretch adhesions or when stiff-walled cavities indicate the necessity for positive pressure for actual compression.

The theory of action of artificial pneumothorax in promoting the healing of tuberculous lesions has been explained in a number of different ways. The factors involved have been listed by Pinner as (1) rest of the collapsed lung, or part of it, (2) elastic relaxation of pulmonary tissue, (3) alteration of the circulation of blood in the lung—relative anemia, (4) alteration of the gaseous metabolism of the lung—anoxemia, and increase in carbon dioxide, (5) stasis of lymph, and (6) cessation of spread in the collapsed lung.

A consideration of these factors will reveal their relative therapeutic significance. First, rest of the collapsed lung, or part of it is readily demonstrated. The respiratory motions of the lung are dependent upon the motion of the chest wall and diaphragm on the one hand and upon the intrapleural negative pressure and atmospheric pressure on the other. As long as the respiratory muscles perform their function and the intrapleural pressure is subatmospheric, or negative, at any point in the respiratory cycle there will be some ventilation and some motion of the lung. This fact can be readily demonstrated under the fluoroscope or by comparison of X-ray films taken both at inspiration and at expiration. Further proof is found in the fact that in bilateral pneumothorax the two lungs maintain normal gaseous exchange. Therefore, pneumothorax, as it is usually done, does not afford any very great reduction in the respiratory motions of the lung as a whole. However, in regions of diseased pulmonary parenchyma the elastic tension is increased, and when the lung relaxes, due to the reduction in its volume, these regions retract more than the normal tissue. This is readily demonstrated by the so-called selective collapse. In the selective collapse the site of the lesion may be almost or quite completely collapsed while the rest of the lung remains well aerated. While perhaps not the dominant factor, this is undoubtedly an important one in promoting healing in tuberculosis.

The second is elastic relaxation of the pulmonary tissue. When the lung is collapsed its total volume is reduced and the elastic tension is reduced or eliminated. Thus the natural tendency of scar tissue to contract is favored and the traumatizing effect of continuous high tension is abolished. Since cavities are held open principally by the elastic tension of the surrounding tissue, elimination of this tension allows the walls of cavities to approximate. All of these conditions are favorable to healing. Therefore, elastic relaxation must be considered an important factor in promoting healing in pneumothorax.

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* Read before the Section on Internal Medicine of the Society, November 27, 1936.

The third factor is alteration in the circulation of blood in the collapsed lung. It has been observed experimentally that the flow of blood in the lungs increases during inspiration and decreases during expiration. Since the total lung volume is increased during inspiration and decreased during expiration, there seems to be a parallelism between the total lung volume and the flow of blood in the lung. In pneumothorax the lung volume is reduced. Therefore, a relative anemia exists in the collapsed lung. This has been said to exert a stimulating influence on fibrosis and in this way to favor healing of the tuberculous lesions.

The fourth factor is alteration of the gaseous metabolism of the lung. There is serious doubt that this factor plays any important part. While there is probably a minor deficiency in the oxygenation of the arterial blood in pneumothorax, it is inconceivable that a degree of anoxemia sufficient to exert a bactericidal effect on the tubercle bacilli could ever exist in a therapeutic pneumothorax. The most that could be expected is that the slight relative anoxemia and increase in carbon dioxide that is produced might be less favorable for the growth of the tubercle bacilli than the normal tension of oxygen and carbon dioxide in the lung.

The fifth factor, stasis of lymph, is a pretty well accepted fact. The flow of lymph is slower in a collapsed lung than in a fully expanded one, and this reduces the absorption of toxic material. Stasis of lymph also promotes the formation of fibrous tissue and is, therefore, a significant factor in the healing of tuberculous lesions.

The sixth factor is cessation of spread in the collapsed lung. The reduction of the blood and lymph flow in the collapsed lung diminishes the chance of spread by these routes. The tortuous course of bronchi and the diminished flow of air in the collapsed lung reduce spread by the bronchogenic route.

Due to the tremendous respiratory reserve with which nature has provided man, the physiological effects of induced pneumothorax as far as respiration is concerned are of little or no significance provided there is a reasonable amount of normal pulmonary parenchyma remaining. As has been said, pneumothorax as it usually is done does not entirely eliminate ventilation of the normal lung parenchyma. It has been estimated that a normal person at rest uses only about 10 or 15 per cent of his respiratory capacity, so that even a complete collapse of one lung or a 50 per cent collapse of both lungs leaves a considerable reserve. In fact, experience has shown that this reserve is in many cases sufficient to insure comfort under the conditions of normal activity.

Collapse of one lung does not cause the other lung to dilate or hypertrophy. In fact, in many patients the mediastinum is flexible and the pneumothorax causes it to shift to the opposite side, encroaching upon and actually reducing the volume of the expanded lung.

The vital capacity is reduced somewhat by pneumothorax. However, according to Pinner the percentage decrease in vital capacity is considerably less than that in residual air. For this reason the reduction in vital capacity is considerably less than the amount of air which is injected to produce the collapse.

Pneumothorax exerts an effect upon the circulation which in the presence of a markedly impaired circulatory system might prove dangerous. The reduction in the size of the pulmonary capillary bed increases the resistance in the lesser circulation and in the presence of a lowered myocardial reserve this may be sufficient to cause an acute dilatation of the right side of the heart. This has occurred twice in my experience. The intrathoracic negative pressure exerts a suction influence upon the great veins in the thorax which promotes their filling. This negative pressure is reduced by pneumothorax, and in the presence of an impaired circulatory system collapse by this method may cause increased venous pressure with edema of the extremities and dyspnea out of proportion to the extent of the pulmonary collapse.

However, the physiological effects of pneumothorax upon a normal circulatory system are not significant and in no way impair its usefulness as a therapeutic measure.

The effect of the use of pneumothorax as a therapeutic measure upon the economic problem presented by tuberculosis is one of its most outstanding advantages both from the standpoint of the patient and that of the community. Frequently the appearance of tuberculosis in a family, especially if the victim is the breadwinner, means that the family's income is cut off until the victim can return to work. Without the use of pneumothorax this usually means a period which is frequently measured in years. With pneumothorax the period of disability is often a matter of only a few months, and in a few selected cases can be eliminated entirely. Ambulatory pneumothorax treatment is now a procedure of established worth. From the standpoint of the community it means that indigent patients in whom pneumothorax is used have to be maintained in public hospitals for shorter periods and the time during which their families have to be provided for by public or private charity is reduced.

The effect of the use of pneumothorax in tuberculosis upon the public health is equally significant. It is an accepted fact that many patients who would surely die from tuberculosis under the more conservative forms of treatment are restored to health by pneumothorax. Thus the mortality rate is reduced. Many patients who for one reason or another can not be kept in isolation can be rendered sputum-free, or their sputum can be made free of tubercle bacilli by collapse of their diseased lung or lungs. Thus the danger of spreading the disease from them is eliminated and the morbidity rate is reduced.

As to the indications for the use of artificial pneumothorax in pulmonary tuberculosis it may be said that it is indicated in every case of proved activity unless there is present some contraindicating condition, or unless some other form of collapse therapy is preferable. There are some patients who get well on bed rest alone, but there are no reliable criteria for distinguishing these from patients who will continue to progress in spite of bed rest. Pneumothorax will bring about a cure in many of the latter. Therefore, if we would do the greatest good to the greatest number, we should give all the benefits afforded by pneumothorax.

The most frequently encountered contraindication to this form of treatment is too extensive involvement of both lungs. If the lungs are so extensively involved that the respiratory reserve is markedly reduced, it would be obviously unwise to further decrease it by collapse of the lungs. Because of the physiological effect of pneumothorax upon the circulatory system, any gross impairment of that system is a contraindication. Asthma and advanced emphysema are contraindications for evident reasons. Miliary tuberculosis is not benefited by pneumothorax. Extensive extrapulmonary tuberculosis frequently renders the outlook for recovery so hopeless that it would be futile to attempt pneumothorax. However, improvement in the pulmonary condition is followed by improvement of the extrapulmonary disease in many cases. In general it may be said that any coexisting condition which seriously impairs the life expectancy of the patient is a contraindication to artificial pneumothorax.

Among the factors which interfere with the success of treatment by this form of collapse therapy, the most frequent is an adherent pleura. When extensive this may prevent any collapse at all. Even when some degree of collapse can be obtained, adhesions may prevent sufficient collapse to be of therapeutic value. Adhesions prevent any collapse at all in about 25 per cent of all cases in which pneumothorax is attempted and interfere with the success of the treatment in about 25 per cent of those in whom collapse is obtained.

The commonest complication which occurs is the development of pleural effusion. This happens in about 75 per cent of the cases. The cause of these effusions is still debatable. In many cases they are small and soon disappear spontaneously, requiring no treatment. Others may require one or more aspirations before subsiding. Rarely a simple effusion may develop into a tuberculous empyema or become secondarily infected with pyogenic organisms. Pleural shock due to injury to the pleura is a very rare occurrence. Air embolism occurs infrequently as a result of injecting air into a vein in a punctured lung. Superimposed spontaneous pneumothorax occurs occasionally but is usually not a serious complication. In general it may be confidently said that serious complications rarely occur when proper care and judgment are used in the administration of artificial pneumothorax. The advantages of this form of treatment so greatly outweigh the risks attending its use that the latter may be disregarded.

There are certain accessory measures used in artificial pneumothorax treatment which deserve some comment. The first of these is intrapleural pneumolysis by which interfering adhesions are cut. This is a minor procedure, and by means of it many cases which are being rendered unsuccessful by adhesions are made successful. Another is phrenic nerve interruption by which the diaphragm is temporarily or permanently paralyzed to relax adhesions or to afford more rest to the collapsed lung. A third is oleothorax. This consists of the injection of some inert mineral or vegetable oil fortified by gomenol, a vegetable antiseptic. By means of this many cases of persistent effusion or even tuberculous empyema can be controlled.

In conclusion, artificial pneumothorax has attained a position of paramount importance in the treatment of pulmonary tuberculosis. When confronted with an active case of this disease, the problem is not so much whether one should do artificial pneumothorax as it is whether he is justified in omitting it. It has proved to be the means of recovery in many otherwise hopeless cases and has greatly shortened the period of disability in many others. Unless definitely contraindicated there seems to be no valid reason for withholding it in any case of active pulmonary tuberculosis.

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Prerenal Azotemia and the Pathology of Renal Blood Flow.—Deficient urinary elimination with resultant azotemia and uremia results not only from intrinsic disease of the kidneys and urinary passages, but may also be a reflection of pathological processes in other parts of the body. From the point of view of the sequence of events in the elaboration of the urine, one may speak of nitrogen retention of the latter category as *prerenal azotemia*—in contradistinction to renal azotemia due to primary disease of the kidneys and postrenal azotemia resulting from obstruction of the urinary passages. This discussion will be confined to the renal and prerenal azotemias, leaving the nitrogen retention that so often results from lesions of the urinary passages to the urological section of the program. . . .

Occurrence of the Prerenal Azotemias. 1. Severe and protracted vomiting, such as is encountered in pyloric and intestinal obstruction and hyperemesis gravidarum. In chronic intestinal obstruction without vomiting but with accumulation of enormous volumes of intestinal contents in the dilated loops of gut, the nonprotein nitrogen of the blood may rise. In the uremia of organic renal disease, vomiting may add a prerenal to the renal factor in the causation of the azotemia.

2. Immoderate loss of intestinal contents in diarrhea or rarely duodenal fistula. Azotemia of this origin occurs commonly in infants but is rare in adults, apart from cholera, unless there is complication by vomiting so that the lost fluid and salt is not replaced.

3. In certain affections of the liver and biliary passages. Not very rarely, when convalescence seems smoothly initiated after operations on the gallbladder or common duct, after an interval of from 1 to 6 or even more days, malaise develops, the temperature rises, oliguria sets in, the nonprotein nitrogen of the blood rises, the patient becomes restless and then perhaps delirious or comatose, and may succumb with the clinical picture of uremia. A similar picture has been observed following traumatic pulpification of the liver and may occur during acute liver degeneration or in acute exacerbations of chronic liver disease. While marked degeneration of the renal tubules may be found at necropsy, in other cases, despite azotemia and the clinical picture of uremia, little morphological change in the kidneys is demonstrable. The syndrome just described has been spoken of as the "hepato-renal syndrome" or "liver death," and is one of the chief dangers of those undergoing gallbladder surgery.

4. In diabetes with acidosis, either in coma or precoma, or in the complete absence of cerebral symptoms with only such complaints as weakness or loss of weight, marked nitrogen retention may be found. The azotemia may continue to mount after the patient has been brought out of coma by insulin. Significant azotemia is present in about half of comatose diabetics. The azotemia usually occurs only after a protracted period of acidosis with polyuria and rarely in previously well controlled diabetics who have gone into coma rather abruptly as a result of cessation of insulin or an infection.

5. In the crises of Addison's disease there is a rise in the nonprotein nitrogen of the blood. The same occurs in much more pronounced degree in experimental removal of the suprarenal glands and is so characteristic that it has served as a means for testing the potency of cortical extracts.

6. In traumatic shock the nonprotein nitrogen of the blood often rises to considerable heights.

7. In postoperative collapse (surgical shock) there may be pronounced azotemia.

8. In the circulatory collapse of pneumonia, diphtheria, sepsis, peritonitis, and other infections, the nonprotein nitrogen of the blood may attain high levels.

9. In widespread burns with shock, there may be great azotemia.

10. In coronary thrombosis with shock, the nonprotein nitrogen occasionally rises notably and may exceed 100 mg. per cent. Nitrogen retention was present in 5 of 6 fatal instances of myocardial infarction studied by Steinberg.

11. Following profuse hemorrhage, notably from the gastro-intestinal tract, azotemia may appear and even surpass 100 mg. per cent of nonprotein nitrogen. Alsted found the blood urea increased in 12 of 25 patients with hematemesis and melena. . . .

Abstract of article by Arthur M. Fishberg, M.D., New York City, *Bulletin of the New York Academy of Medicine, December, 1937, p. 710.*

WASHINGTON'S FIRST DIABETIC CAMP FOR CHILDREN

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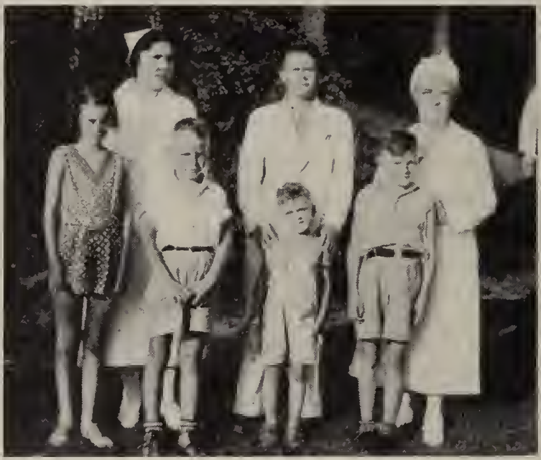
Washington's first diabetic camp for children was operated at the Christ Child Society Farm for Convalescent Children, Rockville, Maryland, from August 1, to August 29, 1937, inclusive. Five children, aged 5 to 12 years, were in attendance.

In addition to the regular personnel of the Farm, one adult male diabetic patient was employed as councilor, and much of the routine diabetic care of the children, such as the weighing of food, urinalysis, injection of insulin, keeping of diabetic records and general supervision of the activities of the diabetic children, were placed in his hands. One graduate nurse was also assigned for diabetic nursing care. The authors supervised the diabetic treatment of the children, making 3 or more visits to the Farm each week.

Miss Mary Davis, Dietitian of the Georgetown University Hospital, was in charge of the diet kitchen. It was due largely to her conviction that there was a real need for a diabetic camp for children that Washington owes its first project of this kind. Her zeal inspired others to aid in this work.

The Christ Child Society coöperated in every way possible to make the camp a success, and we are especially appreciative of the help rendered by Dr. Robert A. Bier, attending physician, and Miss Mary Kennedy, superintendent of the Farm.

Summer camps for juvenile diabetics are relatively new aids in the treatment of this type of patient. A number of camps have been established in New England and there are others scattered throughout the country. So far as known none are nearer to Washington than Philadelphia and Cleveland. On the basis of questionnaires sent out by various groups here and in other cities, it is estimated that there are probably fewer than 100 known white diabetic patients under 21 years of age in Washington and vicinity. It would appear that a fair proportion of the white underprivileged diabetic children between the ages of 6 and 12 years were given the advantages of the Christ Child Farm for Convalescent Children this summer. When one considers that a diabetic child's activities are definitely restricted because such individuals must be under constant supervision by some responsible person in the family (usually the mother) more or less constantly, it follows that such children will have little possibility of partaking of the vacations and freedom in the country of the so-called normal child. Add to this the fact that the mother is likewise tied down with the responsibilities of testing urine for the presence of sugar, injecting insulin and weighing food, in addition to her natural concern for her offspring, and one can readily understand what a repetitious and worrisome existence the life of a diabetic and his parent must be. Hence the need of a place in the country where the child can be as other children are—with them, but supervised by adequate medical and nursing care. Likewise, the mother can take a much needed rest and vacation even though she does nothing but remain at home.



Children at Diabetic Camp and Nursing Personnel, Christ Child Farm

The results of treatment at the Diabetic Camp are summarized in the accompanying table.

Four of the 6 patients were undernourished on admission and all of these gained from 1 to 9 pounds during their stay. The 6 patients made an average weight gain of 3.45 pounds.

With the exception of 1 child, the urine of each was examined qualitatively for sugar and acetone before each meal and at bedtime. Occasional quantitative tests were also run. Estimations of the amount of sugar in the blood were also made on all patients at least twice a week.

All of the patients received protamine zinc insulin with supplemental doses of unmodified or crystalline insulin at breakfast time. With the exception of 1 patient the insulin dosage was increased during the period of observation.

NAME	AGE	SEX	NUMBER OF DAYS AT CAMP	WEIGHT		INSULIN DOSAGE ON ADMISSION		INSULIN DOSAGE AT DISCHARGE		DIET						REACTIONS	COMPLICATIONS
				Admission	Discharge	Regular	Protamine	Regular	Protamine	On admission			At discharge			1 mild 2 moderate 3 semicoma 4 comatose	
										C	P	F	C	P	F		
R. W.	22	M	29	119.50	128.50	8	40	10 crystalline	44	185	83	104	185	83	104	Several 1 Few 2	Cold during last week
H. R.	12	F	29	64.50	67.50	10	36	9	44	154	74	86	165	84	97	One 1	Toothache on 2nd day Sore throat on 25th day
B. S.	10	M	29	66.25	66 00	10	20	8	26	149	56	76	159	69	101	Several 1	Cold and sore throat during last 2 weeks
R. F.	5	M	24	40.00	41.00	0	5	0	10	102	47	110	102	47	110	None	Acute otitis media during last 10 days
B. L.	11	M	23	64.50	67.75	8	36	0	36	218	84	125	216	92	133	Many 1 Several 2 Two 3	Cold during last week
N. P.	8	F	14	56.50	57.50	0	24	4	32	186	60	72	186	60	72	None	Nostalgia

Reactions in 3 of the patients were not uncommon and 1 patient who had always been insulin-sensitive had 2 severe reactions.

During the last week of the camp a mild upper respiratory epidemic affected all of the diabetic patients and many of the nondiabetics because of confinement indoors because of rain. The only serious complication was an acute otitis media, which responded to appropriate treatment.

The children's activities were not restricted and except for their eating a weighed diet in a separate dining room, the examination of urine for sugar and the administration of insulin, their lives were not different from those of the nondiabetic convalescent children at the farm. It was our idea to have these diabetic children mingle and play with the nondiabetics as much as possible in order that they might be able to feel that there was little difference between their outlook on life and that of their nondiabetic playmates.

The diabetics received instruction in weighing out their prescribed diets, examination of the urine for sugar and injection of insulin.

As a result of their vacation at the diabetic camp the youngsters returned to their homes in better physical condition than when they left, with a better idea of their responsibilities as diabetic patients, and with a knowledge that in spite of their disease, their activities need not be very different from those of nondiabetic children.

We believe that the results obtained at the first diabetic camp held for the children of Washington and vicinity compare favorably with those held in other sections of the country and warrant the operation of a similar camp next summer. It is to be hoped that a larger number of underprivileged diabetic children will have the opportunity of partaking of its benefits, and also that a similar camp for diabetic children of a higher economic status will be established.

A STUDY OF THE TEMPORARY USE OF THERAPEUTIC DOSES OF BENZEDRINE SULFATE IN 147 SUPPOSEDLY NORMAL YOUNG MEN (MEDICAL STUDENTS)*

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In recent medical literature considerable interest has been manifested in the pharmacological properties and therapeutic uses of benzedrine (beta-amino-propyl benzene or benzyl methyl carbinamine). Benzedrine is a compound of the epinephrine series resembling ephedrine in chemical constitution, as shown by Barger and Dale in 1910, who made an exhaustive study of a large group of epinephrine-like substances, and a large number of amines that have an action simulating that of the sympathetic nervous system stimulation of epinephrine. These investigators because of this similarity of action termed these substances sympathomimetic amines. The sympathomimetic action of the compounds is responsible for the dilatation of the pupils and bronchi, for vasoconstriction and the pressor effect, and for the cardiac stimulation. The best known of the clinical actions of benzedrine and similar preparations are the diminution of congestion of the nasal mucosa, the maintenance of blood pressure in spinal anesthesia and in orthostatic hypotension, and the relief of spasm of the gastro-intestinal tract. More recently the stimulating effect on the central nervous system has been employed in cases of narcolepsy, mental depressions, postencephalitic Parkinsonism, psychoneurosis, and chronic exhaustion. The most striking effect of the drug is its prolonged and marked stimulation of the nervous system without toxic side-effects or habit-forming properties in the doses commonly employed.

Having become interested in this drug we desired to determine for ourselves what effects it would have in therapeutic doses on supposedly normal young individuals. The results of recent studies concerned with the central action of benzedrine should be mentioned. After a study of the use of the drug in a number of individuals of normal psyche and of various types of mental derangement, Davidoff and Reifenstein drew the following conclusions: (A) Benzedrine sulfate is apparently more stimulating to normal persons than to depressed or self-absorbed patients. (B) It is more effective in increasing the motor activity, the speech activity and the general efficiency than in elevating the mood. (C) It is of more value in the organic depressions, particularly the alcoholic than in those of psychogenic origin. (D) It may be of value in differentiating the states of depression due to alcohol alone, which are usually rapidly dissipated by the drug, from the states of alcoholic depression superimposed on and masking depressions of psychogenic origin, which do not respond readily to the drug. (E) It may render depressed or self-absorbed patients more accessible to investigation or psychotherapy. (F) It may be of use in reducing weight. (G) The beneficial effects of benzedrine sulfate therapy may be counterbalanced by untoward reactions occurring in the course of the administration. This drug should be employed with caution and under favorable circumstances. (H) Benzedrine sulfate apparently may accelerate the rate of improvement in cases in which ultimate recovery is likely to be an inevitable result.

Conclusions of Nathanson in clinical observations of the central action of benzedrine are of interest in connection with our study. They are as follows: (1) Beta-amino-propyl benzene (benzedrine) produces in most individuals a definite stimulation of the central nervous system in doses which do not result in a peripheral sympathomimetic action. (2) Euphoria, a feeling of exhilaration, lessening of fatigue, an increased energy and capacity for work, and talkativeness follow quite regularly the administration of from 10 to 20 mg. of the drug. (3) Although the drug has its most striking effect in narcolepsy it acts favorably in states of persistent exhaustion and in individuals who become easily fatigued; the reactions observed indicate that patients who are in a depressed state may be benefited. (4) Studies on normal individuals indicate that benzedrine increases energy and efficiency to a degree that the drug should be of value in the preparation of individuals for activities that require an increased expenditure of physical and mental energy. Along the same lines the clinical observations of Wilbur, MacLean and Allen of patients with states of chronic exhaustion, depression and psychoneurosis are of interest. The immediate effects of the oral administration of benzedrine to their group of 100 patients who had been diagnosed as having chronic exhaustion, depression and psychoneurosis were benefited to approximately 80, 70 and 46 per cent, respectively. In some instances the results were stated to be spectacular. However, the effects of continued administration of the drug were less favorable. Of the patients initially benefited, about 50 per cent of those who had chronic exhaustion and 25 per cent who had depression continued to have benefit from periods of 1 to 8 months. These investigators concluded that benzedrine is a stimulant and therefore apparently does not fundamentally and permanently alter a psychotic disorder or a state of chronic exhaustion. They did not believe that the question as to whether it is logical and safe to continuously stimulate individuals who present such disturbances can be answered at present.

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Some recent experiments have been performed on the acuity of individuals undergoing mental tests. In well controlled experiments Sargent and Blackburn found that the ratings of individuals undergoing such tests were 8 per cent higher when given benzedrine.

Method of Study

In order to study the immediate effects of benzedrine sulfate in therapeutic doses on supposedly normal individuals, we called for volunteers from among the sophomore and senior classes of medical students in this institution. There were 151 volunteers, none of whom knew with any degree of certainty what drug or drugs they were receiving. Approximately half of the students were given first 10 mg. benzedrine tablets to take after breakfast and after lunch for 3 days; the other half were given tablets of lactose of the same size and shape to be taken similarly. Then, after a period of 5 days the preparations were reversed, but the students were not informed that they were receiving other kinds of tablets. Altogether, 147 took the benzedrine tablets and all 151 took the lactose tablets. The following questionnaire was given each student to fill out:

Before: Pulse .... Respiration ....
Blood Pressure ....
Third Day: Pulse .... Respiration ....
Blood Pressure ....
1. Did you notice any effect from these capsules? ....
2. If so, what was the chief effect? ....
....
3. Were you made fatigued, peppy, or did you feel about as usual? ....
....
4. Was there any change in mood (depression, exhilaration, etc.)? ....
5. Were you more talkative? ....
6. Did they affect your concentration? ....
7. Were you "nervous"? ....
8. Did you have dryness of the mouth or excessive salivation? ....
....
9. Did you notice either drowsiness or insomnia? ....
10. Was there any effect upon your appetite? ....
11. Did you have any other reactions? If so, what and when? ....
....
12. Would you like to continue taking this preparation?
....
Signed: ....

All of the 147 students who took the benzedrine tablets reported reactions of some kind from the use of the drug. Only 16 of the 151 students who took the lactose reported reactions thought by them to be due to it.

Results of Study

Changes in pulse rate. The pulse rate on the afternoon or evening of the third day of taking the benzedrine tablets was reported to be more than 10 beats faster per minute than it had been before taking the tablets by 99 of the 147 students. The greatest increase was 40 beats per minute, and the average was 15 beats per minute.

Effect on respiration. An increase in the rate of respiration was noted by only 5 students of the 147. One student complained of dyspnea.

Effect on blood pressure. Of the 147 students only 64 reported on the state of the blood pressure before and after taking benzedrine. Thirty-four of the 64 noted an increase of more than 10 mm. Hg. in the systolic blood pressure after taking the drug. One student observed an increase of 40 mm. Hg. in the systolic pressure. On the whole the systolic pressures increased more than the diastolic pressures.

Chief effects of benzedrine sulfate. The following list shows the chief effects and their frequency from the use of the drug in the 147 students:

Psychic stimulation	71
Insomnia	28
Nervousness	13
Palpitation of heart	6
Headaches	4
Vertigo	3
Dryness of the throat	3
Fatigue	2
Depression	2
Euphoria	2
Epigastric pain	1
No effect	2

Answers to questions 3 to 12, inclusive. In answer to the specific question "did you feel fatigued, peppy, or as usual," 113 stated that they felt peppy. In answer to question 4 as to any change in mood, 72 students reported that they became exhilarated. Forty-two students answered question 5 to the effect that they became more talkative. In answering the question as to the effect on concentration, 61 reported that they had an increased power of concentration while taking the drug and 8 reported a decrease in power of concentration. In answer to the question "were you nervous," 81 stated that they were more nervous. Seventy-six students reported dryness of the throat in answer to the specific question. One hundred and twenty-six students suffered from insomnia, and 57 students reported decrease in appetite. The answers to the question as to the occurrence of other reactions may be listed as follows:

Headaches	19
Polyuria	16
Palpitation of the heart	14
Flushing of the face	5
Vertigo	5
Dilatation of the pupils	4
Sense of precordial constriction	4
Epigastric pain	4
Depression following drug	3
Catharsis	3
Constipation	2
Sense of fullness in the head	2
Sense of throbbing in the head	2
Uneasiness	2
Weakness of the legs	2
Chilling of the limbs	1
Blurred vision	1
Pain in the legs	1
Dyspnea	1
Fatigue	1
Sweating	1
Nausea	1

Only 38 students expressed a desire to continue using the drug, and 80 per cent of these qualified this answer by stating that they would like to use it at time of examinations and when it was necessary to stay awake.

CONTRAINDICATIONS TO THE USE OF BENZEDRINE

For the sake of safety we wish to emphasize the fact that certain definite contraindications to the use of benzedrine sulfate have been recognized: (1) Hypertension, (2) coronary arteriosclerosis, and (3) a state of manic excitement. It is probably best not to use the drug in any but the mildest cases of cardiac or vascular disease. Davidoff and Reifenstein believe the drug should be used with considerable caution under the following circumstances: (A) Idiosyncracies to small doses or the early appearance of alarming untoward effects, (B) more severe forms of vasomotor instability, (C) wide daily fluctuations in blood pressure or pulse rate, (D) tendency to physical over-activity as observed in the agitated depressions, (E) history of previous excitement as in catatonic dementia praecox, epilepsy, and mental deficiency, (F) history of suicidal and homicidal tendencies, (G) history of convulsive seizures, (H) anorexia, (I) insomnia, and (J) malnutrition and states of exhaustion, debility and lowered bodily resistance.

Indications for the Use of Benzedrine

The following is a list of uses for which benzedrine has been advocated: (1) As a local astringent, (2) narcolepsy, (3) persistent states of fatigue (nervous exhaustion), (4) post-encephalitic Parkinsonism, (5) arterial hypotension, (6) gastrointestinal spasm, (7) overdoses of barbiturates, (8) preparation of individuals for periods of unusual mental or physical exertion, (9) as an adjunct to the action of atropine, stramonium, and scopolamine, and (10) attacks of migraine.

Summary and Conclusions

Benzedrine sulfate in doses of 10 mg. twice daily was administered for 3 days to a group of 147 medical students who did not know the nature of the drug they were taking. As a control they were given at another time similar tablets containing only lactose, the nature of which they likewise did not know. The most striking results were a temporary increase in energy in 113, temporary exhilaration and feeling of well-being in 72, and increased power of mental concentration in 61. Insomnia was produced in 126 students and various unpleasant symptoms in a large number. However, there were no serious ill-effects. It would appear that the use of the drug might be permitted or even prescribed for normal individuals who suffer from lack of self-confidence or mild depression and who deem it advisable to temporarily overcome these drawbacks. Similarly the drug might be permitted in tested individuals who are required to engage in tests requiring mental alertness or perhaps competitive physical activities. However, whenever the drug is used it should be understood by the individual that it is only an emergency measure and that after the emergency has passed an adequate period of rest must be available. The drug is apparently not conducive to the formation of a habit. Although it is apparently not dangerous except when certain pathologic conditions exist, it would appear that the dose of 20 mg. a day is probably too much for the average normal individual because of the insomnia and other unpleasant side-effects so often observed when this dosage is employed.

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Clinic on Meningococcemia with Vegetative Mitral Endocarditis (Subacute Bacterial Endocarditis); With Findings at Postmortem Examination.—*History.* The patient, a man aged 56 years, was admitted to the Clinic and the hospital on November 4, 1935, because of recurrent attacks of fever associated with sweating, weakness and loss of weight. Inquiry into the family history revealed no significant facts. He had always been well except for an attack of tonsillitis and quinsy 10 years before. A year and a half before admission to the Clinic a right hydrocele had developed which had been aspirated on two occasions.

The present illness apparently began 8 months before admission to the Clinic with an acute febrile condition that was said to have been influenza. In addition to fever, the patient complained of pain in both knees. The knees were swollen, and while in the hospital in his home community, they were aspirated and clear yellow fluid was obtained. He remained in the hospital under observation for 10 weeks. After leaving the hospital he was weak, slept poorly and had little appetite, but whether or not he had fever at this time could not be determined from the history. During the summer he had continued to lose weight and strength and had complained of frequent night-sweats. Pain in both knees and the calves of the legs continued to be troublesome when he walked.

At the time of the patient's admission to the Clinic and hospital he appeared acutely ill, had irregular fever which went up to 101°F, sweating, chilly sensations and moderate dyspnea on slight effort. . . .

Postmortem Examination. The heart weighed 402 Gm. On the epicardial surface, chiefly over the right ventricle, were patches of fibrinous exudate of the type encountered in uremic pericarditis. . . . Microscopically, the vegetations consisted of thrombi heavily interspersed with polymorphonuclear leukocytes and clusters of bacteria. The valve leaflet itself was partly necrotic. There was also a marked fibroblastic reaction in the leaflet at various points of attachment of the vegetation. The base of the valve and the underlying myocardium were uninvolved. The bacteria proved to be gram-negative cocci when stained by the Brown-Gram method. The pericardial exudate consisted almost entirely of loosely attached fibrin. The sub-epicardial capillaries were dilated and there was some margination of leukocytes. . . .

Comment. The literature now contains numerous references to cases of meningococcic endocarditis, in some of which complete recovery occurred. Some of the reports stress the fact that clinical evidence of meningitis was completely absent and it was presumed that the organism had gained entrance into the blood stream without involving the meninges.

In the case reported herein, we could not find any clinical evidence of a previous meningitis and the physician who attended the patient during the early part of his illness had observed no signs or symptoms suggestive of this disease. Careful neurologic examination revealed no signs of meningitis. The spinal fluid was not examined for fear of precipitating meningitis. However, the demonstration of meningeal changes at postmortem examination makes us conclude that this patient had suffered from meningitis which was not severe enough to produce the usual symptoms. It is interesting and of course unusual for the meningococcus to behave in this manner, that is, to produce minimal changes in the structures most susceptible to its invasion and to take root and flourish in the endocardium, a tissue which apparently in most instances is quite resistant to the meningococcus. . . .

Abstract of Case Report by F. A. Willius, M.D., Section on Cardiology and L. M. Eaton, M.D., Section on Neurology, *Proceedings of the Staff Meetings of the Mayo Clinic, December 1, 1937, p. 762.*

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SICKNESS INSURANCE NOT THE REMEDY

Voluntary sickness insurance, intended to spread and reduce the costs of medical care and make better medical service available to families of low income, seems logical at first glance. However, the physicians who have recently joined philanthropists and social workers in endorsing such a plan should look more searchingly at the system they propose. In every instance in which a nationally organized medical profession has unwittingly adopted a prepayment plan for altruistic reasons and to prevent socialization or nationalization of medicine, government control of medical practice has resulted, the plan has been made universal and compulsory, its motives have been degraded, and physician, patients and government have suffered.

In the United States most of the arguments advanced in favor of sickness insurance are economic. More than one half of the families in this country now have incomes of less than $2,000.00 a year. It is stated that such incomes do not afford adequate medical service without deprivation of other essentials for health and happiness. Obviously in this case the fault is economic rather than medical, and, far from relieving economic burdens, sickness insurance for such people increases them.

Costs of medical services cannot be estimated in advance; a single epidemic can invalidate all calculations of medical costs. Moreover, medical services are not commodities, they cannot be evaluated beforehand in terms of cash, and whenever this has been attempted miscalculation of the insurance risks has produced either an increased national economic burden or degradation of the quality of medical service. One of the greatest secondary costs of sickness insurance results from increasing morbidity. This increase is apparent in the insurance records of England and Germany and can be ascribed mainly to lowered standards of medical care, lack of lengthy personal contact between physician and patient, and the conscious or subconscious desire on the part of some patients to obtain a return for money already spent.

The immediate costs of administration of sickness insurance are great. In England, for example, where a prepayment plan has existed long enough to allow introduction of every possible saving in cost of administration, such cost closely approaches the amount paid as fees to physician-participants. In most nations endorsing or compelling sickness insurance it has been found that the number of administrators equals or exceeds the number of physicians. Obviously, the only means for meeting these immediate costs is by government subsidy, since increasing the rate of insurance surely defeats the mission of such plans to reduce medical costs for the insured. Therefore, it is hard to believe that any government agency in this country could have the temerity to foster a scheme of sickness insurance, knowing that such action must increase the national debt and thereby add more taxes to an already creaking economic system.

Sickness insurance as a panacea for the difficulties of the low-income group is a dismal failure. In the end the ones who stand to suffer most by such insurance are the patients whose care it designs. They find that the financial bargain they have made on the basis of life, death, and health is insecure. Standardization and reduction in physicians' fees make it necessary for the physician to increase the volume of practice. Insurance systems, by doubling or trebling morbidity as in England and Germany, make this increase easy, and the physician spends most of his time imperfectly treating minor illnesses by tongue, pulse, and bottle methods. Diagnosis and personal counsel, which are the basis of most medical practice, are lost; preventive medicine falters; and standards of medical care decline.

If sickness insurance is provided by government legislation or is contributed to, even partly, by government funds, it comes necessarily under government control by political appointments and bureaus of administration. Even though the system be instituted by the organized medical profession, government control is a logical consequence, and the physician is dominated. Similarly, when sickness insurance becomes compulsory, as it must if it is to be wide-spread, patients too are subject to its domination. The patients' money is spent in the way the administrators of the system think best, and experience in other countries indicates that this is a sure way to lower standards of living and health for physicians and patients alike.

Postgraduate training for the physician is devoted to instruction in bookkeeping, execution of insurance and sickness records and reports, criteria for statements of illness, and means of reducing costs by use of inexpensive and often less effective drugs. Clinical research by the average practicing physician, the results of which form so large and valuable a part of our own medical literature, is stifled when his energies are absorbed in caring for persons with minor and imaginary illnesses and in other activities entirely foreign to medical service.

Finally, it must be remembered that the Principles of Medical Ethics of the American Medical Association are an expression of custom which may or may not need remedy, that such remedy can appear only by slow evolution if chaotic effects are to be avoided, and that by its inherent revolutionary character sickness insurance is not the remedy.

H. H. H.

MEMBERSHIP

Membership increase is most desirable. While maintaining all of the necessary standards for a constituent body of the American Medical Association, the number of applicants accepted has exceeded previous years. Well should this be. The Society gains, but above all the individual practicing medicine who has the necessary qualifications adds prestige and opportunity for scientific advancement obtainable in no other way. Each member should constitute himself as a membership committee, getting a supply of blanks from the Society's Office. As an instance of what may be done, Dr. Joseph F. Elward, has through his own initiative brought in 22 applications from individuals who belonged in organized medicine. This example should be many times emulated.

TRANSACTIONS OF THE WASHINGTON SOCIETY OF PATHOLOGISTS

The meeting of the Washington Society of Pathologists was called to order at 1:30 P.M., Saturday, November 6, 1937, in the Army Medical Museum by the President, Dr. Oscar B. Hunter. There were 20 members present.

Drs. George Tolstoi, Thomas H. Tomlinson, Luther H. Snyder, A. W. Eaton, and Captain R. M. Thompson were elected as associate members.

Presentation of Cases

Dr. J. W. Lindsay presented the case of a 56-year-old white woman who complained of a growth at the tip of the spine. The patient first noted this growth about 3 years before, with pain and discomfort about the tip of the spine. The pain was relieved on standing and was aggravated on sitting or lying. She has had an X-ray film and claimed the growth had eroded the bone. Pelvic examination revealed a tumor separate from uterus, tubes and ovaries. Coccygeal cyst was suspected. She was operated on, October 16, 1937, under avertin and cyclopropane. An incision was made over the right buttock just to the right of the midline and it extended down to the groove or fascia. The posterior wall of the sacrum was eroded away and a large cyst the size of a man's fist presented; it was filled with mucus and black semi-solid material. The cyst was vascular and encroached upon the rectum anteriorly rendering complete removal of the cyst wall dangerous. The wound was packed open with paraffin, gauze and iodoform packing. Laboratory studies showed a secondary anemia of 3,000,000; otherwise they were negative. The course in the hospital was uneventful. Paraffin sections of the tumor show that there is a fibrous tissue framework in the form of branching trabeculae in which are numerous spicules of bone. In the meshes of this framework there is a loose, cellular structure frequently having a definite papillary arrangement. The structure is associated with a homogeneous pink to slightly purple staining matrix, presumably mucoid in character. There is marked vacuolization of this cellular tissue. A well-defined fibrous capsule appears to surround the larger portions of this tumor although it cannot be definitely determined whether the growth is completely encapsulated externally. The process appears to be a papillary epithelial growth, with marked secretion of mucus. Nothing is found by which its exact source may be determined. The tumor is classed as of low-grade malignancy. Clinical study and X-ray are reported to definitely indicate that there is no connection between the ovary or bowel and the tumor. The arrangement of the tissue in relation to the mucoid matrix on microscopic examination in many places suggests a picture seen in mucoid tumors of the salivary gland. The possibility that this growth has originated from a rest or is a part of a teratomatous growth in or near the sacrum must be considered. The diagnosis is papillary carcinoma (mucoid).

In the discussion the mesoblastic characteristics and the similarity of the histologic picture of chondroma and liposarcoma were noted.

Dr. H. E. Ragle presented the case of a 59-year-old white man who came into the hospital on May 20, 1937, in an advanced state of emaciation. The patient's father had died from a similar condition at the age of 65 years. A past history was not obtainable because of patient's deteriorated mental state and aphonia. The health record indicated that present chorea began in 1924 and had gradually progressed to the present state. Physical examination revealed an emaciated elderly man with marked athetoid contortions, so severe that bed boards had to be placed to keep him from falling out. He was unable to stand. Numerous abrasions were present on his arms and legs where he had injured himself by swinging his arms. Physical and neurological examinations were otherwise essentially negative. The mouth was edentulous. The heart and lungs were negative. He was unable to talk or to swallow. The mental state was undetermined, although it is believed that patient was markedly deteriorated. The sedimentation index was 12 Mm. in 60 minutes. The Kahn test was negative. The patient's condition did not improve with forced feedings and nursing care. Considerable sedation was required to lessen the body contortions. He gradually became weaker, bulbar symptoms progressed, and death occurred at 12:35 P.M., on May 31, 1937. Autopsy revealed extreme emaciation, bronchopneumonia and dehydration. The brain cortex appears fairly normal. The capillaries throughout the brain substance are congested. There are areas of what appear to be degeneration in the region of the neostriatum, particularly in the caudate nucleus and putamen, which is the dark part of the lenticular nucleus. Microscopic sections of the brain show considerable thickening of the small arteries, and in a few places the walls show a heavy infiltration of calcium and iron pigment. There is marked atrophy and gliosis of the caudate nucleus and putamen, but elsewhere the changes are mild, except that the motor regions show no change. The findings in this case check very well with the changes in Huntington's chorea. The pathological diagnosis is Huntington's chorea.

In the discussion it was noted that athetoid movements plus a family history of the disease allow strong presumption of the diagnosis of Huntington's chorea. Histopathologically, there are usually early death of the cells of the caudate nucleus and putamen, overgrowth of the glia making the tissue yellow and spongy, and atrophy of the cortical ganglion cells. In this case there are numerous amyloid bodies which are outside of the ganglion cells, thus differentiating the picture from that of amaurotic family idiocy.

Dr. Walter Freeman presented the case of a white woman with a brain tumor. The brain was well hardened and maintained its shape satisfactorily. It was cut by a midline sagittal incision and revealed on the mesial surface of the hemisphere a moderately dilated third ventricle and lateral ventricle with a rather markedly dilated aqueduct. The anterior and middle commissures were somewhat stretched, but on the whole the cerebrum appeared to be fairly normal. The cerebellum, on the other hand, showed the vermis almost completely displaced by a large lobulated tumor about 6 by 5 cm. in diameter, quite sharply circumscribed, almost encapsulated, oval, firm, grayish, covered over by small pinpoint cavities of somewhat darker color, suggestive of vessels rather than areas of necrosis. In places the capsule was stained yellowish to orange, and more of this discoloration was found about the base of the brain and to some extent even over the cerebral cortex. There was marked flattening of the pons and medulla, but less involvement at the midbrain.

One half of the brain was preserved for mounting and submitted to Dr. R. M. Choisser of the Department of Pathology, George Washington University School of Medicine. The other half was submitted to further sectioning. The cerebrum appeared normal. There was no obvious atrophy of the convolutions or widening of the fissures and only a little dilatation of the ventricles. The basal ganglia appeared normal. Horizontal sections through the brain stem and cerebellum revealed that the tumor preserved its main characteristics, being firmly lobulated and sharply circumscribed and extending out into the hemispheres of the cerebellum to about 4 cm. on each side. Most of the white matter in this way was compressed and only a little cortex around the outside seemed to cover over the tumor. The dentate nucleus was markedly stretched and flattened out and the roof nucleus of the eye could not be identified. Both the brachium pontis and the brachium conjunctivum seemed to be thinned out, and the restiform body was markedly thin and displaced.

Microscopic examination shows the tumor to be very cellular and composed of cells of fairly uniform size and shape with slightly oval nuclei, containing a moderate amount of chromatin, tending to be arranged in solid masses with only occasional ring-like grouping of cells, suggestive of pseudorosettes. None of these are about vessels and there are no acini. There are a small connective-tissue stroma, reaching out from the blood vessels, but apparently there are no glia fibers holding the tumor together. On the other hand, in certain places the cells of the tumor, with the rather vesicular nuclei, are gathered into clumps, separated by what appear to be connective tissue with small dense nuclei and rather suggestive of the architecture of certain pinealomas. There are no areas of calcification or necrosis.

The tumor must have been rather slowly growing on account of the development of cerebellar symptoms before the signs of pressure, and the involvement of the dentate and other nuclei as well as of the vermis must have given rise to the first symptoms. It is remarkable that such a large tumor could develop in the cerebellum without causing more in the way of pressure, and without giving rise to choked discs and increase in the cerebrospinal fluid pressure. The tumor is of a rather unusual type, but the cells agree most closely with the type found in the ependyma and it is probably one of the solid ependynomas. The diagnosis was ependynoma of the fourth ventricle with mild internal hydrocephalus.

In the discussion, the similarity of the histologic picture to that of a pinealoma, and even more to a medulloblastoma because of the closely packed oval cells, the presence of pseudorosettes and a framework with a moderate amount of reticulum fibers was considered. It was pointed out that against the diagnosis of medulloblastoma were the well differentiated characteristics of the cells, the solidity, the well delimited border and the vascularity, and that clinically medulloblastoma of adults generally occurs in the cerebral hemispheres.

Drs. George Tolstoi and Oscar B. Hunter presented the case of a 30-year-old white woman who had a fairly firm mass about midway between the hip and knee on the lateral aspect of the thigh. It was not attached to the skin and was not freely movable. There was no tenderness or fluctuation. The mass was noted in August, 1937, for the first time, watched for several weeks, and appeared to increase slightly in size. It was removed in September, 1937. The postoperative diagnosis was lipoma.

In the discussion the tumor was considered an infiltrating sarcoma, probably neurogenic in origin, but also suggestive of rhabdomyosarcoma.

Dr. R. M. Choisser presented the case of a colored man, aged 28 years, whose symptoms began 2 years before with loss of appetite, indigestion, and vomiting which occasionally contained blood. Gastric analysis revealed total acidity 135° with no free hydrochloric acid. X-ray study of the gastro-intestinal tract showed a filling defect of the duodenal cap; otherwise it was negative. Duodenal ulcer was diagnosed. The patient was placed on a modified Sippy diet and was relieved of all symptoms. He gained about 10 pounds but his symptoms returned when the diet was not followed. He was not seen again until he entered the hospital complaining of pain in the stomach and vomiting of blood. He stated that he had had hematemesis 3 or 4 times during the past 2 years and had lost about 30 pounds. The patient was acutely ill and his abdomen markedly rigid and tender. The blood pressure was 90/60; the temperature 101°F., and the pulse rate 140. A right rectus incision was made and the peritoneal cavity drained of about 1 quart of fluid and pus which had a gastric odor. The white blood cells numbered 5,500, the segmented 35 per cent, the band forms 45 per cent, the lymphocytes 19 per cent, and the monocytes 1 per cent. He died the following day with a terminal temperature of 104°F. Necropsy revealed a ruptured duodenal ulcer and a scirrhous carcinoma of the stomach.

In the discussion the high total acidity and achlorhydria were noted. The histologic picture was that of a linitis plastica and it was stated that "all cases of syphilis of the stomach are found to be cancer if one cuts enough sections."

Dr. Lester Neuman presented the case of a 15-year-old white girl who had a metatarsal bone tumor that had resulted in a pathological fracture. The Wassermann reaction was negative. The X-ray films showed very rapid growth over a period of a month. Section showed a cartilaginous tumor with myxoid elements.

In the discussion chrondromyxosarcoma and benign chondroma were considered. The clinical and roentgen-ray evidence pointed more to a malignant change, while the histologic picture was that of a rather well-differentiated tumor. The difficulty of prognosis from histologic appearance and the fact that a mature cartilage is sometimes found in metastatic cartilage tumors was noted. The consensus of opinion was that the tumor was chondromyxosarcoma.

Dr. Walter Freeman presented the case of a 39-year-old white man who had had a tumor of the meninges measuring about 10 cm. in diameter. Death occurred after operation. There was no invasion of the skull. The microscopic slide showed densely packed polyhedral cells and moderate vascularity.

In the discussion the question of malignancy was considered. Since the bone was not invaded and there was little anaplasia, and although the cells were rapidly growing, it was held that the tumor was probably benign.

Dr. Margaret M. Nicholson presented blood smears from the case of a middle-aged white female physician who, after several days of general malaise suspected a blood dyscrasia, because she had recently heard several lectures on the subject. She discovered a white plaque in her mouth, immediately associated it with agranulocytosis and went to Providence Hospital where numerous blood studies were made. The total white blood count was 1,000. The red blood cells, platelets and hemoglobin showed little change. The differential count showed 99 per cent mononuclears that were generally considered lymphocytes.

In the discussion only one observer felt that the mononuclear cells were other than lymphocytes; this observer interpreted some of the cells as being myelocytes. The majority favored the diagnosis of agranulocytosis.

The meeting adjourned at 4:15 P.M.

CALENDAR FOR COMING MEETINGS

Wednesday, January 5: Stated Meeting. Reports of committees, election of members, etc.

Wednesday, January 12: Joint meeting with the Section on Gastro-enterology.

1. "The Surgery of Peptic Ulcer, Its Indications and Results." Charles Stanley White, M.D.
   Discussion: Brigadier General R. T. Metcalf, Walter Reed General Hospital.
2. "Some Erroneous Concepts Encountered in the Practice of Gastro-enterology." John L. Kantor, M.D., New York City.

Wednesday, January 19: Joint meeting with the Section on Pediatrics. Subject: *Preventive Pediatrics*

I. Growth and Development.
  1. "Nutritional Standards for Normal Growth." James M. Moser, M.D.
  2. "The Recognition of Early Deficiency States of Nutrition." Charles A. Schutz, M.D.

II. Communicable Diseases.
  1. "Studies in Vaccination of New-born Infants: Intradermal Vaccination with Cultivated Virus (Rivers) Compared with Intradermal Vaccination with Diluted Calf Lymph Virus in 1,000 Babies." H. H. Donnally, M.D., Margaret M. Nicholson, M.D., W. S. Anderson, M.D., and M. H. Grosvenor, M.D.
  2. "What May Be Done in the Prevention of Common Contagious Diseases." William F. Burdick, M.D.

Wednesday, January 26: Joint meeting with the Section on Ophthalmology and Otolaryngology.

"Middle Ear Infections." John R. Page, M.D., Surgeon-Director, Manhattan Eye, Ear, and Throat Hospital, New York City.

Section on Internal Medicine, which meets on the fourth Friday, announces Dr. Benjamin Rones as the essayist for the January meeting. Subject: "The Eye in Diabetes." Dr. George R. Minot of Boston follows as a speaker in February before a joint meeting with the General Society on the 16th. He will have for his subject "Anemias: Etiology, Diagnosis and Treatment." These papers are outstanding and undoubtedly will bring a large attendance. Attention of all Society members is called to the opportunity of appearing on the program before this Section. Communicate the titles of proposed papers to Dr. R. Lomax Wells, Chairman, at the earliest possible date.

Annual Scientific Assembly, Medical Society of the District of Columbia, will be held May 4 and 5, 1938. This meeting, which represents the climax of the Society's year, is expected to have all of the educational features of a postgraduate course as well as the social opportunities that have made the first week in May outstanding in Washington medical annals. Dr. W. W. Chase, 1801 Eye Street, N. W., is the general chairman. In the January issue of the Annals full committee personnel and other features of the meeting will be given.

NEWS AND PERSONALS

The American Board of Internal Medicine will hold its next written examination on Monday, February 14, 1938, in various centers of the United States and Canada. This examination is for determination of candidates for the practical examination to be given in San Francisco, June, 1938. The final date for filing applications in the office of Dr. Walter L. Bierring, Chairman, Suite 1210, 406 Sixth Avenue, Des Moines, Iowa, for this written examination is January 15, 1938. For further particulars and application blanks address the Chairman of the Board.

Washington Academy of Surgery meets December 10, 1937. Program:

"Surgery of the Heart and Pericardium." I. A. Bigger, Professor of Surgery, Medical College of Virginia.

American Psychoanalytic Association will hold its 39th meeting at the Hotel Shoreham, December 27–28, 1937. Open meeting will be held on December 27, at 2 P.M., in the Supper Club Room. Subject: "Psychoanalysis and the General Hospital," H. Flanders Dunbar, M.D., New York City. Other papers include:

"Pain as a Psychosomatic Problem." Felix Deutsch, M.D., Boston.

"The Psychoanalytic Study of a Case of Chronic Exudative Dermatitis." Leo Bartemeyer, M.D., Detroit.

"Psychosomatic Reactions to Psychotherapy." Frieda Fromm-Reichmann, M.D., Rockville, Md.

"Poetry Production as an Emergency Defense of Anxiety." H. Levey, M.D., Chicago.

Dr. Lucile Dooley, a member of the Medical Society of the District of Columbia, reads a paper, "A Genetic Study of the Relation of Humor to Masochism," at the closed meeting, December 28.

The Jacobi Society of Washington announces the following election of officers for the year 1937–1938: Harry A. Spigel, *President;* Bernard Notes, *Vice President;* Isadore Levin, *Secretary;* Aaron Nimetz, *Treasurer.*

Washington Ophthalmological Society meets at the Episcopal Eye, Ear and Throat Hospital, January 3, 1938, at 7:30 P.M. The program:

I. Case Presentations:
  1. "Keratoconus with Contact Lens. Blue Sclerotics." C. A. Swanson, M.D., United States Naval Dispensary.
  2. "Unilateral Choroidal Atrophy." Joseph Dessoff, M.D.
  3. "Retinoblastoma—Five-week Old Infant." H. E. Allen, M.D.
  4. "Spontaneous Reattachment of a Detached Retina." Franklin H. Maury, M.D.
  5. "Congenital Lagophthalmos—Mechanism?" Frank D. Costenbader, M.D.

II. "Practical Aspects of the Fitting of Contact Lens, with Demonstration of Technic both from the Lens Trial Case and with Dentacol Impressions." Mr. T. E. Obrig, New York City.

Washington Academy of Medicine has submitted for a coming issue of the Medical Annals, interesting and instructive papers presented at a recent meeting. The Academy's active membership is comprised of accepted practitioners within the medical profession and also from outstanding scientists working in allied fields. It thus occupies a unique position among Washington organizations in that it gives an opportunity for qualified candidates to affiliate with an interprofessional society of high standing.

CORRESPONDENCE

The Status of One of the Four Hundred and Thirty

November 8, 1937.

Dr. Thomas E. Neill, President,
Medical Society of the District of Columbia,
1824 Massachusetts Avenue, N. W.,
Washington, D. C.

Dear Dr. Neill:

As you know, I have always been unalterably opposed to socialized medicine and since I feel that I have been put in a false position concerning it, I am enclosing herewith a copy of my letter to Dr. John M. Peters, Secretary of the Committee of Physicians.

Very truly yours,
(Signed) G. W. Leadbetter

November 8, 1937.

Dr. John M. Peters, Secretary,
Committee of Physicians,
789 Harvard Avenue,
New Haven, Conn.

Sir:

I have not conferred with any person concerning the publication of the proposals as set up by the Committee, therefore, all that follows in this letter is my own opinion.

When I signed the proposals presented to me by Dr. Robert Osgood in Lincoln, Nebraska, last June, I was told that these proposals were to be presented to the American Medical Association at the annual meeting. I understand that this was done and that the Association turned down the proposals. So far so good. From that point on I feel that my signature was obtained under misrepresentation by the proposer inasmuch as there was no suggestion that the proposals were to be given to the lay press. This is a great mistake as I am sure many men will observe after reading the various editorials of yesterday, especially those in the Hearst papers. To wash the soiled linen of a political controversy in public is to say the least degrading and not commensurate with the dignity of the profession. To have referred these proposals to the various medical societies for their action would have been quite sufficient to have obtained their assent or dissent. Whether or not we see eye to eye with our colleagues in their various researches into the subject of socialized medicine (and I for one do not believe in socialized medicine) is beside the point.

I have practiced medicine for several years happily and I think with average good skill and do not propose to become party to guerrilla political warfare or a member of a separatist group. I intend to stand squarely behind organized medicine as represented by the American Medical Association, to obey its dictates in so far as they are within reason. I was and I am in accord with some of the proposals made and, in my own mind, do not believe they represent socialized medicine, but the method of approach is the butt of my attack. The proposals should go through the normal channels and if there are enough men sponsoring it, it should be considered again at the House of Delegates of the American Medical Association.

It is true that the health of the Nation is the government's responsibility, but only so far as preventive medicine is concerned. It is likewise true that research institutions, medical schools and even private institutions may be much benefited by federal, state or private funds, but these funds must be unhampered by the vileness of political intrigue. It is also true and I believe the strongest point in the whole proposal that the American physicians should take the initiative and make their own proposals as to the adjustment of medical practice in a society of unrest.

By the unpardonable error of resorting to the cheap politics of publicity, the proposals, so far as I am concerned, have forfeited the right to my signature and you will please withdraw it from the list.

Very truly yours.
Guy W. Leadbetter, M.D.

REPRINTS RECEIVED

The following reprints have recently been received for which due acknowledgment is made:

"Venereal Diseases of the Anus and Rectum." Garnet W. Ault, M.D., American Journal of Syphilis, Gonorrhea, and Venereal Diseases, July, 1937.

"Malignancy of the Pancreas." Everett Monroe Ellison, M.D., Medical Record, November 3, 1937.

"Recurrent Regional (Terminal) Ileitis." Joseph P. Shearer, M.D., and James T. Jackson, M.D., Annals of Surgery, September, 1937.

Anthony Abraham Deep, M.D.

(1898–1937)

Dr. Anthony A. Deep, who was graduated from George Washington University School of Medicine in 1924, died suddenly on December 12, 1937. He had served variously on the staffs of Emergency and Children's Hospitals. He was born in Brazil, December 5, 1898. He became a member of the Medical Society of the District of Columbia on May 10, 1928.

Funeral services were held on December 14, with burial in Fort Lincoln Cemetery. Dr. Deep is survived by his wife, Mrs. Nazla Samara Deep; two sons, Anthony, Jr., and William.

William Charles Fowler, M.D.

(1864–1937)

Dr. William C. Fowler, whose service with the District of Columbia Government began in 1894, becoming in 1906 Director of Contagious Disease Service and later Health Officer in 1918, was a member of the Medical Society of the District of Columbia since 1889; in 1930 he was made a life member. His death occurred on November 19, 1937, following an operation at the Johns Hopkins Hospital for the relief of tic douloureux.

Dr. Fowler was born in Washington on November 24, 1864. He was graduated in medicine in 1888 from Georgetown University School of Medicine. He had served the Society as First Vice President (1927) and on the following committees: Cancer, Civic Health, Medical Practice Act, Poliomyelitis, Public Information, Toxin-antitoxin. During his official life he tried always to coöperate in the fullest with the aims and ideals of the organized profession. His service as Secretary-Treasurer of the Commission on Licensure under the Healing Arts Practice Act was particularly notable.

His scientific-society memberships included: American Medical Association; American Public Health Association; Anatomical Board of the District of Columbia, which he served as President; Tuberculosis Association; and the Social Hygiene Society.

In masonry he was Past Grand High Priest of Royal Arch Masons of the District of Columbia; Past Master of Lebanon Lodge, F.A.A.M.; Past High Priest of Lafayette Chapter, R.A.M., and a member of Washington Commandery, Knights Templar.

Dr. Fowler is survived by his wife, Mrs. Laura A. Jaques Fowler; two brothers, J. Edward Fowler, and Chapman W. Fowler; and two sisters, Miss Helen Z. Fowler and Miss Belle Fowler, of this city. His funeral was held Monday, November 22; interment in Glenwood Cemetery.

William Essex Whitson, M.D.

(1874–1937)

Dr. William E. Whitson, who was graduated from Columbian (now George Washington) University School of Medicine in 1898, and who became a member of the Medical Society of the District of Columbia on October 4, 1899, died December 3, 1937, at the George Washington University Hospital. A native of Baltimore, the son of the late William A. and Julia M. Whitson, he received his preliminary education in the Washington public schools. After obtaining his degree in medicine he served on the house staffs of Emergency, Washington Asylum (now Gallinger) Hospitals, and the Home for Incurables. During the World War Dr. Whitson was a medical officer in the United States Army. He was active in masonry being a life member of St. John's Lodge, F.A.A.M., a Royal Arch Mason, and a Knights Templar.

Funeral services were held December 6, with burial in Rock Creek Cemetery. He is survived by a sister, Miss Belle M. Whitson, and two brothers, J. Edmund Whitson and Walter I. Whitson, all of this city.

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